

J Pharm Bioallied Sci. 2021 Apr-Jun; 13(2): 230–237.

PMCID: PMC8291112

Published online 2021 May 26. doi: 10.4103/jpbs.JPBS_542_20:

PMID: [34349484](#)

10.4103/jpbs.JPBS_542_20

Metformin Use in Gestational Diabetes: Awareness, Attitude, and Practice among Healthcare Professionals in Malaysia

[Nur Aizati Athirah Daud](#),¹ [Syed Ghouse Mohiuddin](#),¹ [Yi Ping Ong](#),² [Faridah Yusof](#),³ [Fadhleena Yusoff](#),⁴ [Sabariah N. Harun](#),¹ and [Siti Maisharah S. Ghadzi](#)¹

¹Discipline of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Gelugor, Malaysia

²Department of Pharmacy, Hospital Pulau Pinang, Georgetown, Penang, Malaysia

³Department of Pharmacy, Hospital Sultanah Bahiyah, Alor Setar, Kedah, Malaysia

⁴Department of Pharmacy, Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan, Malaysia

Address for correspondence: Dr. Nur Aizati Athirah Daud, Discipline of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 USM, Penang, Malaysia. E-mail: aizati@usm.my

Received 2020 Sep 21; Revised 2020 Oct 28; Accepted 2020 Nov 21.

[Copyright](#) : © 2021 Journal of Pharmacy and Bioallied Sciences

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Abstract

Background:

Metformin has been added in the Malaysian clinical practice guideline (CPG) as one of the first-line options in the management of gestational diabetes mellitus (GDM); however, the uptake on this practice among healthcare professionals is unknown.

Objective:

The objective of the study is to determine the awareness, attitude, and practice and their predictors on the use of metformin for GDM among healthcare professionals in Malaysia.

Materials and Methods:

This was a multicenter, cross-sectional study in three tertiary hospitals in Malaysia. Medical doctors and pharmacists working in several departments were invited to participate in a survey using self-administered questionnaires.

Results:

From 350 questionnaires distributed, 225 were completed by medical doctors (43.1%), pharmacists (40.4%), and specialists (7.5%). Less than 30% of them were aware on the option of using metformin as one of the first-line agents in GDM. Education level, department, and profession were found to be associated with the awareness level ($P = 0.016$, $P = 0.004$, and $P = 0.001$, respectively). 70.2% of the respondents showed a positive attitude toward metformin use in GDM. Only 64 (28.4%) of the respondents have prescribed/dispensed metformin for GDM before, although more than half will consider doing so in the future. Having postgraduate qualifications increased the likelihood of having a good awareness (odds ratio [OR]: 2.44, 95% confidence interval [CI] 1.23–4.85) and to consider prescribing/dispensing metformin for GDM patients (OR: 2.27, 95% CI 1.08–4.78).

Conclusion:

Despite a positive attitude toward metformin use in GDM among healthcare professionals in Malaysia, their awareness level on this practice was low as they currently prefer the use of insulin over metformin.

KEYWORDS: *Gestational diabetes, healthcare professionals, Malaysia, oral antidiabetics, pregnancy*

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. The prevalence of GDM has been reported between 7% and 18% of pregnancies worldwide[[1](#)] while about 8%–9% in Malaysia based on the National Obstetric Registry Report 2011–2012.[[2](#)] GDM has been associated with higher maternal and neonatal morbidity and an increased risk of a variety of maternal and perinatal complications, including preeclampsia, cesarean section, macrosomia, shoulder dystocia, birth injuries, hypoglycemia, and respiratory distress syndrome;[\[3\]](#) hence, maintaining glucose level within the recommended target is the main goal of therapy.

In the latest Malaysian clinical practice guideline (CPG) on the management of diabetes in pregnancy in 2017, metformin has been introduced as a safe option of therapy for GDM. Its use has been supported by evidence on its safety and efficacy, which is mostly comparable with insulin.[\[4,5,6\]](#) There were no demonstrable teratogenic effects, intrauterine deaths, or developmental delays reported with the use of metformin.[\[7\]](#) Moreover, follow-up investigations on the children within 2 years of age had demonstrated that metformin exposure during pregnancy is not associated with poorer neurodevelopmental outcomes relative to insulin exposure.[\[8,9\]](#)

Following the latest CPG updates, the uptake of this practice among our healthcare professionals depends on their awareness of this change and their attitude toward it. Although the gold standard of managing uncontrolled GDM after diet therapy and exercise is insulin, metformin may also be considered an option in view of a better compliance profile, less hypoglycemia effect, and lower cost of therapy. Despite the room for improvement, knowledge

on the acceptance of healthcare professionals on the use of metformin in GDM is lacking. Therefore, this study aims to determine the awareness, attitude, and practice on the use of metformin for GDM among healthcare professionals in Malaysia and the associated predictors.

MATERIALS AND METHODS

Study design and study population

A cross-sectional study was conducted using questionnaires involving obstetrics and gynecology (O&G), medical, and pharmacy departments of three tertiary level healthcare institutions in Malaysia: Hospital Sultanah Bahiyah in Kedah, Penang General Hospital (HPP) in Penang, and Hospital Raja Perempuan Zainab II in Kelantan. A total of 350 questionnaires were distributed in equal numbers to three departments in each hospital – pharmacy, O&G, and medical departments. Online version of the questionnaires was also made available. The reason of distributing the questionnaires both using hardcopies and online versions was to provide flexibility and accessibility for study population.

Ethical approval

The study protocol was reviewed and approved by Medical Research and Ethics Committee (MREC) from the Ministry of Health, Malaysia, in accordance with the Declaration of Helsinki 1975, as revised in 2000 (available at http://www.wma.net/e/policy/17-c_e.html). The MREC approval number is NMRR-18-548-39706. Approval was obtained from all heads of departments involved before the data collection. Written informed consent was obtained from all participants together with the questionnaires. The study was conducted between February 2018 and March 2019.

Study instrument

The questionnaire is in English and provided the details of the study, informed consent form, and participants' information sheet [Supplementary Material]. The questionnaire consists of four sections: (a) personal information, (b) awareness on the use of metformin in gestational diabetes mellitus (GDM), (c) attitude toward the use of metformin in GDM, (d) practice in managing GDM. In Section B of the Supplementary Material, there are three available responses (yes, no, not sure), while in Section C of the Supplementary Material, a 5-point Likert scale was used (strongly disagree, disagree, neutral, agree, and strongly agree). The questionnaire was assessed for face-and-content validity by four experts, and a pilot study was performed among 26 individuals (21 pharmacist and 4 medical doctors) from several institutions (Cronbach's alpha for attitude domain, $\alpha = 0.86$).

Respondents are considered to have high awareness level when they answered "Yes" to four or more the questions in Section B of the Supplementary Material. For attitude toward the use of metformin in GDM, answers in Section C of the Supplementary Material were calculated using a sum score of a maximum of 55. Using original Bloom's cutoff point, respondents were considered to have a positive attitude if the score was 80%–100% (44–55 points), a neutral attitude if the score was 60%–79% (33–43 points), and a negative attitude if the score was <60% (<32 points).

Statistical analysis

The responses to questions on awareness, attitude, and practice were reported as frequency and percentage. Continuous variables were expressed as mean \pm standard deviation (SD). For comparison between two groups, Student's *t*-test was used for continuous variables, while Chi-square test was used for categorical variables. Possible factors associated with the awareness and attitudes were determined using binary logistic regressions. Statistical analyses were performed using IBM SPSS Statistics, Version 24 (IBM Corporation, Armonk, NY, USA). A $P \leq 0.05$ was accepted as statistically significant.

RESULTS

Demographics

Among 350 questionnaires distributed, 199 respondents filled and returned the questionnaires while 26 responses were obtained from the online version. [Table 1](#) shows the demographic characteristics of respondents. Mean age (SD) of the respondents was 31.7 (5.7) years. Of 225 respondents, 151 (67.1%) were female, while majority of the respondents were Malay (108, 48.0%). Only few percentages of them were specialists ($n = 17$, 7.6%), while majority were medical doctors ($n = 96$, 42.7%) or pharmacists ($n = 91$, 40.4%). More than 80% of the respondents had worked not more than 10 years.

Awareness on the use of metformin in gestational diabetes mellitus

Of the 225 respondents, 94 (41.8%) had not read the 2017 version of CPG on the management of diabetes in pregnancy [[Figure 1](#)]. Majority of the respondents were aware that insulin is the first-line agent for uncontrolled GDM with diet and exercise, while 24% were unaware that metformin is one of the treatment options. Overall, only 62 (27.6%) of the respondents showed a good awareness on the use of metformin in GDM as suggested in the CPG [[Table 2](#)]. Those who have masters/specialty degree, working in O&G department, and are O&G specialists were found to have better awareness as compared to those with other group categories ($P = 0.016$, $P = 0.004$, $P = 0.001$, respectively).

Attitude toward the use of metformin in gestational diabetes mellitus

Half of the respondents agreed that metformin can be recommended as the first-line therapy in GDM, after diet control and exercise [[Figure 2](#)], while 172 (76.8%) agreed that a better compliance can be achieved with metformin as compared to insulin. Meanwhile, 117 (53%) had agreed that metformin may cause less weight gain risk and the risk of maternal hypoglycemia as compared to insulin.

Overall, majority ($n = 158$, 70.2%) of the respondents showed positive attitude toward the use of metformin in GDM, while 58 (25.8%) were neutral and 9 (4.0%) showed a negative attitude. Education level may have influenced the attitude as higher percentage of those with bachelors' degree tends to have neutral/negative attitude, as compared to those with postgraduate qualifications. However, this association was not statistically significant.

Practice toward the use of metformin in gestational diabetes mellitus

Only 64 (28%) of the respondents have prescribed or dispensed metformin for GDM before, although more than half ($n = 136$, 60.4%) considered doing so in the future. Insulin was the preferred choice, as majority of the respondents have an experience prescribing or dispensing insulin to patient(s) with GDM. Among the respondents who had prescribed or dispensed metformin before, 41 (64.1%) respondents mentioned that metformin was used as the first-line therapy for GDM uncontrolled with diet and exercise. Meanwhile, 22 (34.4%) of them prescribed/dispensed metformin as an additional treatment to insulin.

Among 146 respondents who have never prescribed/dispensed metformin for GDM before, 13.7% of them thought that it was not the common practice or standard protocol in the department or institution, while 7.5% mentioned that metformin is not the first-line agent for GDM. Meanwhile, 6.8% of the respondents gave the reason of questionable safety profile of metformin and another 6.8% with a reason of a better glycemic control with insulin [Table 3].

More than half of the respondents ($n = 136$, 60.4%) would consider prescribing or dispensing metformin for GDM patients in the future. Most popular reasons include (1) "metformin will increase compliance because it is less invasive" ($n = 19$); (2) "metformin was already stated as an option for GDM in the CPG" ($n = 17$); (3) "metformin is shown to be safe when used during pregnancy" ($n = 11$); and (4) "metformin is cost-effective and provides a better management of glycemic control" ($n = 8$). Meanwhile, 17 (7.6%) will not consider prescribing or dispensing metformin, while 70 (31.1%) were undecided. One of the reasons not to consider prescribing metformin, on the other hand, includes the concern on the safety of metformin use in pregnancy ($n = 12$), as the respondents feel the need for more evidence to address this issue.

Regarding the need of a clinical trial on the use of metformin in GDM among Malaysian patients, 175 (77.8%) of the respondents agreed that it is needed. Most of them agreed that it may prove the efficacy and safety of metformin in local population and will improve compliance among the patients. Those who did not agree for a clinical trial thought that there is no need to replicate previous findings in Malaysian population.

Predictors of awareness, attitude, and practice on metformin use in gestational diabetes mellitus

Having postgraduate qualifications and working in the O&G department were associated with good awareness on this issue (odds ratio [OR]: 2.44, 95% confidence interval [CI] 1.23–4.85 and OR: 3.00, 95% CI 1.61–5.48, respectively) [Table 4]. Meanwhile, medical doctors or specialists were 2.5 times more likely to have a good awareness on metformin use in GDM as compared to the pharmacists (OR: 2.53, 95% CI 1.31–4.92). Good awareness on this issue was associated with a positive attitude toward metformin use in GDM (OR: 2.43, 95% CI 2.43–5.02). Meanwhile, those who had postgraduate qualifications are more likely to consider prescribing/dispensing metformin for GDM patients (OR: 2.27, 95% CI 1.08–4.78). At last, healthcare professionals with a good awareness and good attitude regarding the use of metformin in GDM were more likely to consider prescribing/dispensing metformin for GDM in the future.

DISCUSSION

This study showed a poor awareness level among most respondents on the use of metformin as one of the first-line options in managing GDM. However, majority of them had a positive attitude toward metformin use in GDM, although not many have prescribed or dispensed metformin to GDM patients.

More than half of healthcare professionals participated in our study were not aware that the CPG on the management of diabetes in pregnancy was released on 2017 and it included oral antidiabetics as one of the treatment modalities for GDM patients.[10] This can be due to the possibilities of using other international guidelines available, or they are not directly involved in the treatment of GDM. Well-established guidelines produced by the American Diabetes Association (ADA) and American College of Obstetricians and Gynecologist (ACOG) are not supporting the use of oral antidiabetics in GDM as a first-line pharmacological agent, as compared to the National Institute for Clinical Excellence (NICE), as of 2010.[3,11,12] According to the ADA and ACOG, metformin can be given as an adjunct treatment or if the patient was already taking it before they were pregnant, which was already being practiced in Malaysia.

The attitude toward the use of metformin in GDM is generally positive. Majority of the respondents agreed with the statements that metformin may improve the maternal safety profile, weight gain, and fetal outcome, as compared to insulin. In the early days, the safety profile of metformin use during pregnancy in human was inconclusive, as most findings came from observational studies, with small sample size and of variable quality. One of the earliest randomized clinical trials in the treatment of gestational diabetes was the Metformin in Gestational Diabetes (MiG) trial involving 751 women. In this trial, metformin was shown to be comparable with insulin on the risk of perinatal complications, yet it was preferred by the women because it did not require an injection.[13] In addition, positive maternal outcomes were also reported with metformin use, such as reducing maternal pregnancy weight gain and the risk of pregnancy-induced hypertension.[6,14,15,16] More recent studies also found that metformin was not associated with any maternal or fetal complications, except for a slight increase in the risk of preterm birth.[8,17,18,19,20,21,22] Recent meta-analysis studies also reported on the benefits of metformin on fetal outcomes, including lowered risk of neonatal hypoglycemia, large for gestational age babies, and shorter neonatal intensive care unit stay. [5,6,7,23]

The data on long-term outcome on the offspring following the use metformin, however, are limited. A meta-analysis study ($n = 500$ children) had reported a higher body mass index mid-childhood among children exposed to metformin as compared to insulin, although the absolute weights do not differ significantly between both groups.[24] In terms of efficacy, metformin was also shown to be comparable to insulin therapy in controlling blood glucose level in GDM patients.[6,14,16]

Regarding the practice in managing GDM among the respondents, only 27% of the respondents had prescribed or dispensed metformin for GDM previously, especially when the patients were already treated for prepregnancy diabetes. Stopping of metformin treatment during pregnancy may lead to a potential worsening of hyperglycemia and subsequent

complications to both mother and the fetus. The use of metformin in treating GDM may possibly improve compliance and preference among the patients because of the ease of administration, although more studies should be done to confirm this.

Current CPG updates on the use of metformin should be an option to provide optimum care for the patients, by taking into consideration patients' risk profile and preference. At the same time, there is a need for healthcare providers to be equipped with the updated knowledge and proper reasoning for the treatment required. The role of a pharmacist should not be undermined as they play a pivotal role in diabetes management programs. As reported earlier, a clinical pharmacist-assisted program in drug therapy optimization of hyperglycemia among pregnant patients had shown to be effective in improving patient knowledge and disease control.[25] A collaborative effort between doctors, pharmacists, and other healthcare professionals may promote a better patient-centered continuum of care for GDM patients.

Clinical trial in Malaysian population may be useful to inform the healthcare professionals, regarding the efficacy and safety aspects of metformin in treating GDM. Variable results were observed in trials performed in various populations, rendering the need for a local data to support the practice, including studies on potential genetic markers specific for the population. As of now, the uptake of the recommendation on metformin use in GDM among Malaysian healthcare professionals is yet to be well implemented. Regardless, several aspects need to be considered in weighing the risk and benefits of treatment options in GDM, as it may not only affect patient itself but also the short- and long-term effect of the born child. Above all, patients need to be adequately informed on such risks and benefits, to avoid unnecessary fear and to ensure adherence to the treatment and monitoring plans outlined.

Strengths and limitations

The strength of this study is that it was the first to provide a background data on the awareness and practice on the use of antidiabetic agent among pregnant women. This may be useful for future study directions in this field, such as qualitative studies, clinical trials, or pharmaco-economic evaluations. There are two main limitations to this study. First, selection bias may occur as a result from sampling method. Only three departments were selected – medical, O&G, and pharmacy, which might cause a bias toward a good awareness on the topic. However, it is understood that not all healthcare professionals working in those departments are directly involved in the treatment for pregnant patients. Second, newly diagnosed GDM patients are more likely to be treated at the primary care setting (i.e., maternal and child health clinics), which may contribute to the low level of practice in prescribing metformin in GDM patients.

CONCLUSION

Although there was a good level of awareness and a positive attitude toward the use of metformin in GDM among healthcare professionals, the practice still favors the use of insulin over metformin. Healthcare professionals were concerned on the possible maternal or fetal complications that may arise. Therefore, it is crucial for healthcare professionals to be aware of current evidence-based findings in this matter to assist in the risk–benefit assessment of metformin use in GDM, while taking into consideration patients' preference.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Acknowledgments

We would like to thank the head of departments and personnel involved in subject recruitment at the study site. We are also grateful for the willingness of the respondents in participating in this study. Lastly, we would like to thank the Director General of Health Malaysia for his permission to publish this article.

SUPPLEMENTARY MATERIAL

Questionnaire items

Section A: Personal information

1. State your gender (male/female)
2. Which race do you belong to? (Malay, Chinese, Indian, Others)
3. What is your age?
4. Choose your line of work below (endocrinologist, obstetrics and gynecology specialist, family medicine specialist, medical officers, pharmacists, others)
5. What is your highest level of education? (degree, masters/specialty, PhD/subspecialty)
6. How long have you been working in this field? (<10 years, 11–20 years, 21–30 years, >30 years)
7. Which department are you working at? (endocrinology, obstetrics and gynecology, pharmacy)

Section B: Awareness on the use of metformin in gestational diabetes (Yes/No/Not sure)

1. Have you looked into the Clinical Practice Guideline on the Management of Diabetes in Pregnancy (2017)?
2. Insulin is the first line agent for gestational diabetes mellitus (GDM) uncontrolled with diet and exercise
3. Metformin is one of the treatment options for GDM uncontrolled with diet and exercise
4. Metformin is preferred over insulin in GDM uncontrolled with diet and exercise
5. According to the literature, the use of metformin in GDM is not associated with any birth defects, preeclampsia, or any adverse maternal nor fetal outcomes.

Section C: Attitude towards the use of metformin in GDM (strongly agree, agree, neutral, disagree, strongly disagree, neutral, agree, strongly agree)

1. I think metformin has a better safety profile in maternal hypoglycemia as compared to insulin in the treatment of GDM
2. I think metformin has a better safety profile in pregnancy-induced hypertension as compared to insulin in the treatment of GDM
3. I think metformin has a better profile in weight gain as compared to insulin in the treatment of GDM
4. I think metformin has a better safety profile in preterm birth as compared to insulin in the treatment of GDM
5. I think metformin has a better safety profile in neonatal hypoglycemia as compared to insulin in the treatment of GDM
6. I think metformin has a better profile in birth weight as compared to insulin in the treatment of GDM
7. I think metformin has a better profile in neonatal intensive care unit stay as compared to insulin in the treatment of GDM
8. I think metformin is as effective as insulin in the treatment of GDM
9. I think metformin is as safe as insulin to be used in the treatment of GDM
10. I think patients' compliance toward metformin is better than insulin therapy in GDM
11. I think metformin can be recommended as the first-line therapy in GDM.

Section D: Practice in managing GDM (Yes/No/Not sure/Not relevant)

1. Have you ever prescribed/dispensed insulin for a patient with GDM before?
2. Have you ever prescribed/dispensed metformin for a patient with GDM before?
3. If yes [to Question 25], can you explain why?
 - a. As a first line for uncontrolled GDM with diet and exercise
 - b. As an additional treatment with insulin therapy
 - c. As a monotherapy after poor compliance to insulin
 - d. Others, please specify:
4. If no [to Question 25], can you explain why?
5. Will you consider prescribing/dispensing metformin for GDM patients in the future?
6. Do you think a clinical trial on the use of metformin in GDM among Malaysian patients is needed?

REFERENCES

1. Coustan D, Lowe L, Metzger B, Dyer A. The HAPO study: Paving the way for new diagnostic criteria for GDM. *Am J Obstet Gynecol.* 2010;202:654.e1–6. [PMCID: PMC2897007] [PubMed: 20510967]
2. Nalliah S. Gestational diabetes mellitus: National interests using evidence based information. *Med J Malaysia.* 2017;72:1–2. [PubMed: 28255131]
3. American Diabetes Association 14. Management of diabetes in pregnancy: Standards of medical care in diabetes-2019. *Diabetes Care.* 2019;42(Suppl 1):S165–72. [PubMed: 30559240]
4. Feghali MN, Scifres CM. Novel therapies for diabetes mellitus in pregnancy. *BMJ.* 2018;362:k2034. [PubMed: 30012851]

5. Butalia S, Gutierrez L, Lodha A, Aitken E, Zakariasen A, Donovan L. Short- and long-term outcomes of metformin compared with insulin alone in pregnancy: A systematic review and meta-analysis. *Diabet Med*. 2017;34:27–36. [PubMed: 27150509]
6. Kitwitee P, Limwattananon S, Limwattananon C, Waleekachonlert O, Ratanachotpanich T, Phimphilai M, et al. Metformin for the treatment of gestational diabetes: An updated meta-analysis. *Diabetes Res Clin Pract*. 2015;109:521–32. [PubMed: 26117686]
7. Zhao LP, Sheng XY, Zhou S, Yang T, Ma LY, Zhou Y, et al. Metformin versus insulin for gestational diabetes mellitus: A meta-analysis. *Br J Clin Pharmacol*. 2015;80:1224–34. [PMCID: PMC4631195] [PubMed: 25925501]
8. Ijäs H, Väärämäki M, Saarela T, Keravuo R, Raudaskoski T. A follow-up of a randomised study of metformin and insulin in gestational diabetes mellitus: Growth and development of the children at the age of 18 months. *BJOG*. 2015;122:994–1000. [PubMed: 25039582]
9. Ijäs H, Väärämäki M, Morin-Papunen L, Keravuo R, Ebeling T, Saarela T, et al. Metformin should be considered in the treatment of gestational diabetes: A prospective randomised study. *BJOG*. 2011;118:880–5. [PubMed: 21083860]
10. *Malaysia Health Technology Assessment Section. Clinical Practice Guideline: Management of Diabetes in Pregnancy*. United Kingdom: Malaysia Health Technology Assessment Section; 2017.
11. Simmons D, McElduff A, McIntyre HD, Elrishi M. Gestational diabetes mellitus: NICE for the U.S.? A comparison of the American Diabetes Association and the American College of Obstetricians and Gynecologists guidelines with the U.K. National Institute for Health and Clinical Excellence guidelines. *Diabetes Care*. 2010;33:34–7. [PMCID: PMC2797981] [PubMed: 19837790]
12. *NICE-National Institute for Health and Care Excellence. Diabetes in Pregnancy: Management from Preconception to the Postnatal Period*. United Kingdom: NICE Guideline; 2015.
13. Rowan JA, Hague WM, Gao W, Battin MR, Moore MP. Metformin versus insulin for the treatment of gestational diabetes. [Last accessed on 2020 Oct 28]; *N Engl J Med*. 2008 358:2003–15. Available from: <http://www.nejm.org/doi/full/10.1056/NEJMoa0707193>. [PubMed: 18463376]
14. Poolsup N, Suksomboon N, Amin M. Efficacy and safety of oral antidiabetic drugs in comparison to insulin in treating gestational diabetes mellitus: A meta-analysis. *PLoS One*. 2014;9:e109985. [PMCID: PMC4193853] [PubMed: 25302493]
15. Gui J, Liu Q, Feng L. Metformin vs insulin in the management of gestational diabetes: A meta-analysis. *PLoS One*. 2013;8:e64585. [PMCID: PMC3664585] [PubMed: 23724063]
16. Jiang YF, Chen XY, Ding T, Wang XF, Zhu ZN, Su SW. Comparative efficacy and safety of OADs in management of GDM: Network meta-analysis of randomized controlled trials. *J Clin Endocrinol Metab*. 2015;100:2071–80. [PubMed: 25803270]
17. Niromanesh S, Alavi A, Sharbaf FR, Amjadi N, Moosavi S, Akbari S. Metformin compared with insulin in the management of gestational diabetes mellitus: A randomized clinical trial. *Diabetes Res Clin Pract*. 2012;98:422–9. [PubMed: 23068960]
18. Scherneck S, Schlinke N, Beck E, Grupe K, Weber-Schoendorfer C, Schaefer C. Pregnancy outcome after first-trimester exposure to metformin: A prospective cohort study. [Last accessed on 2020 Oct 28]; *Reprod Toxicol*. 2018 81:79–83. Available from: <https://doi.org/10.1016/j.reprotox.2018.07.004>. [PubMed: 30017588]
19. Beyuo T, Obed SA, Adjepong-Yamoah KK, Bugyei KA, Oppong SA, Marfoh K. Metformin versus insulin in the management of pre-gestational diabetes mellitus in pregnancy and gestational diabetes mellitus at the Korle Bu Teaching Hospital: A randomized clinical trial. *PLoS One*. 2015;10:e0125712. [PMCID: PMC4422739] [PubMed: 25945500]

20. Mohammed MA, Kadhim KA, Gasim GA, Fawzi HA. Metformin compared to insulin for the management of gestational diabetic. *Int J Res Pharm Sci.* 2018;9:1063.
21. George A, Mathews JE, Sam D, Beck M, Benjamin SJ, Abraham A, et al. Comparison of neonatal outcomes in women with gestational diabetes with moderate hyperglycaemia on metformin or glibenclamide A randomised controlled trial. *Aust N Z J Obstet Gynaecol.* 2015;55:47–52. [PubMed: 25688819]
22. Given JE, Loane M, Garne E, Addor MC, Bakker M, Bertaut-Nativel B, et al. Metformin exposure in first trimester of pregnancy and risk of all or specific congenital anomalies: Exploratory case-control study. *BMJ.* 2018;361:k2477. [PMCID: PMC6016021] [PubMed: 29941493]
23. Li G, Zhao S, Cui S, Li L, Xu Y, Li Y. Effect comparison of metformin with insulin treatment for gestational diabetes: A meta-analysis based on RCTs. *Arch Gynecol Obstet.* 2015;292:111–20. [PubMed: 25547060]
24. Tarry-Adkins JL, Aiken CE, Ozanne SE. Neonatal, infant, and childhood growth following metformin versus insulin treatment for gestational diabetes: A systematic review and meta-analysis. *PLoS Med.* 2019;16:e1002848. [PMCID: PMC6684046] [PubMed: 31386659]
25. Batta RA, Kasabri V, Akour A, Hyassat D, Albsoul-Younes A. Impact of clinical pharmacists intervention on management of hyperglycemia in pregnancy in Jordan. *Int J Clin Pharm.* 2018;40:48–55. [PubMed: 29134488]

Figures and Tables

Table 1

Demographic data of the respondents ($n=225$)

General characteristics	Respondents, n (%)
Gender	
Male	74 (32.9)
Female	151 (67.1)
Study site	
Hospital Sultanah Bahiyah	64 (28.4)
Hospital Pulau Pinang	83 (36.9)
Hospital Raja Perempuan Zainab II	78 (34.7)
Race	
Malay	108 (48.0)
Chinese	95 (42.2)
Indian	17 (7.6)
Others	4 (1.8)
Age (mean years \pm SD)	31.7 \pm 5.7
Profession	
Medical doctor	96 (42.7)
Pharmacist	91 (40.4)
Obstetrics and gynecology specialist	14 (6.2)
Family medicine specialist	9 (4.0)
Endocrinologist	3 (1.3)
Others	7 (3.1)
Education level	
Degree	181 (80.4)
Masters/specialty	36 (16.0)
PhD/subspecialty	8 (3.6)
Working duration (years)	
<10	183 (81.3)
11-20	33 (14.7)
21-30	7 (3.1)
>30	2 (0.9)
Department	
Pharmacy	91 (40.4)

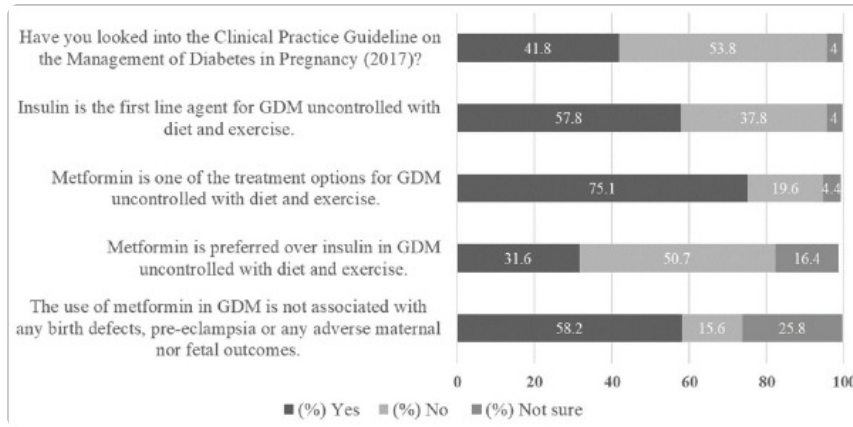
SD: Standard deviation

Table 2

Factors associated with good awareness on the use of metformin in gestational diabetes mellitus

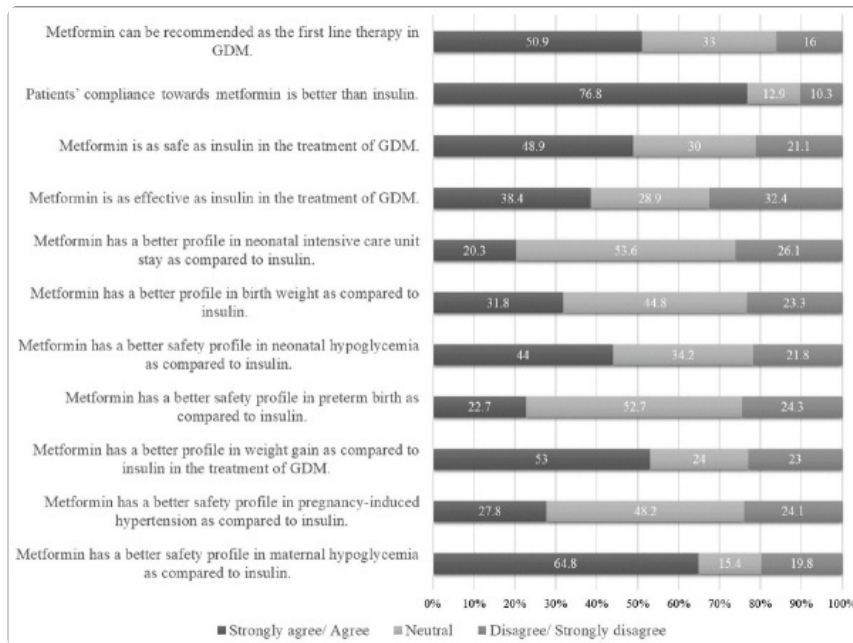
Characteristics	Good awareness* (n=62)	Moderate/Poor awareness (n=163)	P
Study site			
Hospital Sultanah Bahiyah	15 (24.2)	49 (30.1)	0.502 [¥]
Hospital Pulau Pinang	22 (35.5)	61 (37.4)	
Hospital Raja Perempuan Zainab II	25 (40.3)	53 (32.5)	
Age in years, mean (SD)	32.8 (7.1)	31.4 (5.1)	0.117 [€]
Gender			
Male	22 (35.5)	52 (31.9)	0.609 [¥]
Female	40 (64.5)	111 (68.1)	
Race			
Malay	35 (56.5)	73 (44.8)	0.437 [¥]
Chinese	21 (33.9)	74 (45.4)	
Indian	5 (8.1)	12 (7.4)	
Education level			
Degree	43 (69.4)	138 (84.7)	0.016 [¥]
Masters/Specialty	17 (27.4)	19 (11.7)	
PhD/Subspecialty	2 (3.2)	6 (3.7)	
Department			
Obstetrics and gynecology (O&G)	32 (51.6)	44 (27.0)	0.004 [¥]
Medical	13 (21.0)	44 (27.0)	
Pharmacy	16 (25.8)	73 (44.8)	
Others	0	1 (0.6)	
Profession			
Medical doctor	29 (46.8)	68 (41.7)	0.001 [¥]
Pharmacist	16 (25.8)	75 (46.0)	
Obstetrics and gynecology specialist	10 (16.1)	4 (2.5)	
Endocrinologist	1 (1.6)	2 (1.2)	
Others	5 (8.1)	10 (6.1)	
Years of working experience			
<10	53 (85.5)	130 (79.8)	0.088 [¥]

Figure 1



Responses on the items assessing awareness on the use of metformin in gestational diabetes mellitus among healthcare professionals

Figure 2



Responses on the items assessing attitude toward the use of metformin in gestational diabetes among healthcare professionals

Table 3

Reasons for not prescribing or dispensing metformin for patient(s) with gestational diabetes

Reasons	n (%)	Example of comments
Not directly involved in the treatment of GDM	38 (26.0)	-
Not the current practice or standard protocol in the department/ setting/institution	20 (13.7)	<p>“Not routinely used as treatment option in this center for GDM”</p> <p>“Not practiced in this institution”</p> <p>“Patients do well on insulin. I need to change practice and start prescribing after the CPG but have not done so. Still skeptical”</p>
Metformin is not the first line for GDM	11 (7.5)	“First-line treatment for GDM is insulin and usually is well tolerated”
Better glycemic control with insulin	10 (6.8)	“Better glycemic control has been achieved with insulin alone”
Concern about the contraindication and safety profile of metformin	10 (6.8)	<p>“Contraindicated”</p> <p>“Increase risk of birth defect”</p> <p>“Previously metformin said to be teratogenic”</p> <p>“Uncertainty about safety”</p> <p>“I thought metformin cannot be given to pregnant ladies”</p>
Not familiar with metformin use in GDM	9 (6.2)	<p>“Not familiar”</p> <p>“Not comfortable to use as first line, for the time being”</p> <p>“Previously not yet established evidence/recommendation”</p>
Others	18 (12.3)	“Mostly doctor prescribed insulin straight away for GDM patient” “use insulin only”
Total	146 (79.3)	

GDM: Gestational diabetes mellitus, CPG: Clinical practice guideline

Table 4

Univariate analysis on the predictors of awareness, attitude, and practice on metformin use in gestational diabetes among health care professionals

Predictors	n (%)		OR (95% CI)	n (%)		OR (95% CI)	n (%)
	Good awareness	Poor awareness		Positive attitude	Neutral/negative attitude		
Educational level (postgraduate versus bachelor's degree)	19/62 (44.2)	25/138 (18.1)	2.44 (1.23-4.85)	35/158 (22.2)	9/67 (15.5)	1.83 (0.83-4.07)	33/44 (75.0)
Department at work (O&G versus others)	32/61 (52.5)	44/162 (27.2)	3.00 (1.61-5.48)	55/157 (35.0)	21/66 (31.8)	1.16 (0.63-2.13)	46/76 (60.5)
Profession (MD/specialist versus pharmacist)	40/56 (71.4)	74/149 (67.1)	2.53 (1.31-4.92)	80/141 (56.7)	34/64 (53.1)	1.16 (0.64-2.09)	74/114 (64.9)
Good awareness versus poor awareness	-	-	-	51/62 (82.3)	107/163 (65.6)	2.43 (1.17-5.02)	51/62 (82.3)
Positive attitude versus neutral/negative attitude	-	-	-	-	-	-	106/158 (67.0)

O&G: Obstetrics and gynecology, MO: Medical doctor, CI: Confidence interval