ORIGINAL RESEARCH

Clinical Impact of Metformin Therapy on Gestational Diabetes Mellitus and Maternal-Infant Health Outcomes

Wei Luo, BD; Lu Yang, BD; Cenchuan Guo, BD; Yanchun Zhang, BD

ABSTRACT

Objective • This study aimed to assess the impact of metformin treatment on clinical parameters (blood glucose, inflammation, hormone levels) and outcomes for both mothers and infants in cases of gestational diabetes mellitus (GDM).

Methods • A comparative study with a retrospective cohort design was conducted. A total of 96 patients diagnosed with gestational diabetes mellitus over the past three years in our hospital were included. The participants were divided into two groups: a control group receiving insulin treatment and a study group receiving metformin treatment. We compared the clinical effects between the two groups.

Results • After treatment, the levels of postprandial 2-hour blood glucose, fasting blood glucose, and glycosylated hemoglobin significantly improved in both groups compared to pre-treatment levels. Moreover, the study group exhibited superior outcomes compared to the control group ($P < .05$). The levels of interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β) demonstrated improvement in both groups, with the study group outperforming the control group ($P < .05$). Additionally, the levels of Cystatin C (CysC) and Homocysteine (Hcy) in both groups improved post-treatment, with the study group showing better results than the control group ($P < .05$). Notably, the study group exhibited a lower incidence of adverse outcomes than the control group ($P < .05$).

Conclusions • Metformin therapy demonstrated a significant clinical impact on gestational diabetes mellitus. Compared to insulin therapy, metformin showed superior effects on blood glucose, inflammation, hormone levels, and maternal and infant outcomes, suggesting its adoption for patient consideration. (*Altern Ther Health Med.* [E-pub ahead of print.])

Wei Luo, BD; Lu Yang, BD; Cenchuan Guo, BD; Yanchun Zhang, BD; Department of Obstetrics and Gynaecology, Huai'an Hospital, Huai'an, Jiangsu, China.

Corresponding author: Yanchun Zhang, BD
E-mail: llbb17714508263@163.com

INTRODUCTION

Gestational diabetes mellitus (GDM) is a common condition within the realm of obstetrics and gynecology, representing a significant concern for pregnant women.[1] Diabetes emerges as a common complication during pregnancy. Characterized by the onset of diabetes during pregnancy, GDM poses risks not only at an individual level but has also become a growing global health issue. In China, the prevalence ranges from 1% to 5%, while globally, it ranges from 1% to 14% in recent years.[2]

The incidence of gestational diabetes is on a continual rise, drawing increasing attention globally. It poses a severe and detrimental impact on the health of pregnant women, emerging as a high-risk complication during pregnancy.[3] It is imperative to recognize the potential harm gestational diabetes can impose on pregnant women and promptly administer appropriate treatment. Timely intervention is crucial to mitigate the adverse effects of hyperglycemia on both maternal and infant well-being.[4]

In the clinical management of gestational diabetes, pharmaceutical intervention plays a crucial role in line with global medical advancements. Patients diagnosed with gestational diabetes have the option to select from various treatment modalities. Considering the inherent inflammatory response, variations in blood sugar, and hormonal fluctuations in gestational diabetes patients, the outcomes can differ significantly.[2-4] Therefore, determining the optimal treatment strategy for individuals with gestational diabetes mellitus presents a significant challenge as a novel concern in the clinical field.[1-2]

There is a scarcity of literature in determining the optimal treatment for GDM. Therefore, this study was conducted to investigate the impact of metformin treatment on the clinical aspects (blood glucose, inflammation,

hormone levels) and the outcomes for both mothers and infants in cases of GDM. The following sections present the findings of this investigation.

DATA AND METHODS

Study Design

This study employed a comparative study design involving a cohort of 96 patients diagnosed with gestational diabetes mellitus within our hospital over the preceding three years. The cohort was carefully divided into two groups, namely the control group and the study group, to facilitate a comprehensive examination of the effects of metformin treatment on GDM. This study design was ethically conducted with the approval of the institutional review board and in accordance with the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from each participant, ensuring adherence to ethical standards throughout the study.

Characteristics of Participants

The control group, comprised of individuals aged between 23 and 35 years with an average age of 29.22±1.05 years, underwent treatment according to conventional protocols. At the same time, the study group, consisting of participants aged between 24 and 37 years with an average age of 29.26±1.03 years, received metformin treatment. Gestational ages for both groups ranged from 25 to 37 weeks (control group) and 26 to 38 weeks (study group), ensuring a diverse representation. Statistical analysis revealed no significant differences in basic demographic data between the groups ($P > .05$).

Treatment Protocols

Control Group (Insulin Regimen). In the control group, insulin aspartate (SINoptically approved J20150073) manufactured by Novo Nordisk (China) Pharmaceutical Co., Ltd. was employed in this study. The insulin was administered subcutaneously, primarily before dinner, on a once-daily basis for patients. The dosage was carefully controlled, ranging between 0.2IU/kg and 0.3IU/kg per administration. Adjustments to the dosage were permitted based on individual patient conditions, with the flexibility to discontinue the medication upon delivery of the fetus.

Study Group (Metformin Regimen). In the study group, prior to the commencement of metformin, patients also underwent insulin treatment, ensuring uniformity in the treatment approach. This study utilized metformin produced by Sino-American Shanghai Squibb Co., LTD. under the approval number H20023370. The metformin was administered orally with warm water. Initially, patients took the medication twice daily, with each dosage set at 0.5g. Similar to the control group, the administration of metformin was maintained until the delivery of the fetus.

Observation Indices

Blood Glucose Level. Before and after treatment, the study thoroughly observed blood glucose levels in both groups. The primary measurements focused on 2-hour postprandial blood glucose, fasting blood glucose, and glycosylated hemoglobin. Three consecutive measurements were taken for each parameter, and the mean value was calculated and recorded to gauge the fluctuations in blood glucose levels.

Inflammation. Inflammatory conditions were assessed by measuring interleukin-8 (IL-8), tumor necrosis factor-α (TNF-α), and interleukin-1β (IL-1β) levels. Patient blood samples were collected under fasting conditions, with 6ml of peripheral venous blood collected and centrifuged at 3000R/min. The serum obtained was stored for subsequent analysis. IL-8, TNF-α, and IL-1β levels were determined to provide insights into the inflammatory status of the patients.

CysC and Hcy Levels. The study utilized enzyme-linked immunosorbent assay (ELISA) for detecting CysC levels, while homocysteine (Hcy) levels were measured using immunoturbidimetry. Both parameters were recorded to evaluate the corresponding changes in CysC and Hcy levels before and after treatment.

Maternal and Infant Outcomes. Maternal and infant outcomes were categorized into maternal pregnancy outcomes and neonatal pregnancy outcomes. Adverse pregnancy outcomes for mothers included hypertension, preterm birth, and preeclampsia. Similarly, adverse neonatal outcomes encompassing respiratory distress syndrome, neonatal hypoglycemia, and macrosomia were observed and recorded.[4]

Statistical Analysis

The data underwent statistical analysis using SPSS 20.0 (IBM, Armonk, NY, USA). Measurement data were presented as mean ± standard deviation ($\bar{x} \pm s$). The significance of differences between groups was evaluated using the t test for continuous variables, while the χ^2 test was employed for categorical data. Results were expressed as [n (%)] for count data. $P < .05$ was considered statistically significant, indicating a notable difference between the groups under comparison. This careful statistical approach ensured a thorough examination of the data, enabling robust conclusions to be drawn from the study findings.

RESULTS

Blood Glucose Levels Before and After Treatment in the Two Groups

Initially, before treatment, there were no significant differences observed in the 2-hour postprandial blood glucose level, fasting blood glucose level, and glycosylated hemoglobin between the two groups ($P > .05$). After the treatment, noteworthy improvements were witnessed in the 2-hour postprandial blood glucose level, fasting blood glucose level, and glycosylated hemoglobin in both groups. Moreover, the study group exhibited superior outcomes compared to the control group ($P < .05$). Refer to Table 1 for detailed results.

Table 1. Blood Glucose Levels ($\bar{x} \pm s$) Before and After Treatment in Both Groups

Groups	Blood Glucose (mmol/L) 2 h After a Meal		Fasting Blood Glucose (mmol/L)		Glycosylated Hemoglobin [n (%)]	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Study Group (n = 48)	13.22±2.15	8.56±1.12	8.46±1.23	4.85±1.31	8.99±1.23	5.63±1.01
Control Group (n = 48)	13.28±2.11	10.62±1.32	8.47±1.21	6.24±1.23	8.97±1.21	6.97±1.12
t	0.845	7.658	0.695	6.847	0.748	8.254
P value	>.05	<.05	>.05	<.05	>.05	<.05

Note: *t* values represent the statistical *t* test results. *P* values indicate the level of statistical significance. Significance level set at $P < .05$.

Inflammatory Marker Analysis in Pre- and Post-Treatment

Initially, prior to treatment, there were no significant differences in the levels of IL-8, TNF-α, and IL-1β between the two groups ($P > .05$). Following the treatment, notable improvements were observed in the levels of IL-8, TNF-α, and IL-1β in both groups. Furthermore, the study group exhibited superior outcomes compared to the control group ($P < .05$). Detailed results are presented in Table 2.

CysC and Hcy Levels in the Two Groups

Initially, before treatment, there were no significant differences in the levels of CysC and Hcy between the two groups ($P > .05$). After treatment, notable improvements were observed in the levels of both CysC and Hcy in both groups. Furthermore, the study group exhibited superior outcomes compared to the control group ($P < .05$). Refer to Table 3 for detailed results.

Maternal and Infant Outcomes in the Two Groups

In the study group, there were 2 newborns with defects, while the control group had 8. The defect rate in the study group was significantly lower than that in the control group ($P < .05$). Additionally, the incidence of respiratory distress syndrome, hypoglycemia in newborns, and macrosomia in the study group was significantly lower than that in the control group ($P < .05$). Refer to Tables 4 and 5 for detailed outcome comparisons.

DISCUSSION

Gestational diabetes is a common complication during pregnancy that significantly affects both mothers and infants. Uncontrolled blood glucose levels in expectant mothers can create a prolonged hyperglycemic environment for the developing child, potentially inducing lesions in various tissues and organs.[4-5] This prolonged exposure poses a significant risk, ultimately risking the safety of both mother and child. Therefore, timely diagnosis and treatment are imperative for pregnant women diagnosed with diabetes. Immediate intervention is crucial to effectively control blood glucose levels, preventing the occurrence of irreversible damage.[5]

As medical knowledge continues to progress, in-depth investigations into gestational diabetes reveal its correlation with insufficient insulin secretion in pregnant women.[4] This insufficiency results from a disorder in the islet beta cells of pregnant women, preventing the adequate breakdown of blood glucose levels and leading to their accumulation, ultimately inducing gestational diabetes mellitus.[5]

The implications of gestational diabetes for pregnant women are profound, manifesting in various aspects[6]:

Table 2. Two Groups of Inflammatory Conditions ($\bar{x} \pm s$)

Groups	IL-8 (pg/ml)		TNF-α (ng/L)		IL-1β (ng/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment	Before Treatment	After Treatment
Study Group (n = 48).	353.54±39.52	195.52±20.85	29.65±5.12	12.43±2.12	19.16±4.23	7.52±2.23
Control Group n = 48).	353.57±39.54	236.72±28.53	29.68±5.16	19.21±3.21	19.12±4.21	12.36±2.68
t	0.845	7.658	0.695	6.847	0.748	8.254
P value	>.05	<.05	>.05	<.05	>.05	<.05

Note: Inflammatory condition levels are presented in picograms per milliliter (pg/ml) for IL-8 and nanograms per liter (ng/L) for TNF-α and IL-1β. S (standard deviation), IL-8 (interleukin-8), TNF-α (tumor necrosis factor-alpha), IL-1β (interleukin-1 beta), pg/ml (picograms per milliliter), ng/L (nanograms per liter). *t* values represent the statistical *t* test results. *P* values indicate the level of statistical significance. Significance level set at $P < .05$.

Table 3. Two Sets of CysC Levels and Cy Levels ($\bar{x} \pm s$)

Groups	CysC (mg/L)		Hcy (μmol/L)	
	Before Treatment	After Treatment	Before Treatment	After Treatment
Study Group (n = 48)	1.24±0.22	0.61±0.12	13.72±3.52	7.38±1.52
Control Group (n = 48)	1.25±0.23	0.88±0.19	13.76±3.54	9.58±1.76
t	0.843	7.653	0.692	6.846
P value	>.05	<.05	>.05	<.05

Note: This table presents the levels of cystatin C (CysC) and homocysteine (Hcy) before and after treatment in both. CysC levels, measured in milligrams per liter (mg/L), and Hcy levels, measured in micromoles per liter (μmol/L), The *t* values reflect the results of the statistical *t* test, and *P* values indicate the level of statistical significance, set at $P < .05$. The standard deviation ($\bar{x} \pm s$) signifies the variability around the mean.

Table 4. Pregnancy Outcomes [n (%)]in Both Groups

Groups	Number of Cases	Hypertension	Premature Birth	Preeclampsia	Defect Rate
Study Group	48	1 (2.08)	1 (2.08)	0 (0.00)	2 (4.17)
Control Group	48	4 (8.33)	3 (6.25)	1 (2.08)	8 (16.67)
x^2					7.658
P					<.05

Note: This table provides a detailed overview of pregnancy outcomes in both the study group (n = 48) and the control group (n = 48) of pregnant women. The outcomes include the number of cases and the incidence rates (expressed as percentages) of hypertension, premature birth, and preeclampsia in each group. Additionally, the table presents the overall defect rate, calculated as the percentage of adverse outcomes. The chi-square test (χ^2) was performed to assess the statistical significance of the differences observed between the two groups, with a resulting $P < .05$ indicating significance.

Table 5. Pregnancy Outcomes [n (%)] in Both Groups of Newborns

Groups	Number of Cases	Respiratory Distress Syndrome	Hypoglycemia In Newborns	Huge	Defect Rate
Study Group	48	0 (0.00)	1 (2.08)	1 (2.08)	2 (4.17)
Control group	48	2 (4.17)	3 (6.25)	3 (6.25)	8 (16.67)
χ^2					8.457
P value					<.05

Note: This table presents crucial information on pregnancy outcomes in newborns from both the study group (n = 48) and the control group (n = 48). The chi-square test (χ^2) was applied to evaluate the statistical significance of observed differences between the two groups, with a resulting $P < .05$ indicating significance.

(1) Following the onset of diabetic lesions in pregnant women, there is an increase in amniotic fluid within the uterus, creating an excess compared to normal pregnancies. This increase in amniotic fluid may heighten the challenges associated with delivery for pregnant women.[5-6]

(2) The development of diabetes exposes pregnant women to an intensified environment of elevated blood glucose levels, making them susceptible to the induction of lesions in various tissues and organs. The simultaneous occurrence of additional health issues presents a substantial risk to the well-being of both the mother and the child. One particularly common and concerning complication in this context is pregnancy-induced hypertension.[7]

(3) During prolonged periods of elevated blood glucose levels in pregnant women, the fetus is intricately connected to the mother through the umbilical cord, relying on her as the primary source of essential nutrients. This persistent exposure of the fetus to heightened blood glucose levels increases the likelihood of abnormal development, giving rise to complications such as hypoglycemia and macrocephaly. In severe cases, it may lead to the development of severe consequences like mental retardation and cerebral palsy.[8]

(4) As pregnancy progresses, the energy demand of the fetus within the pregnant woman intensifies. This escalating demand can lead to the development of insulin deficiency in the fetus. Additionally, if there is an excessive amount of lipolysis in the pregnant woman, it can heighten the risk of complications such as stillbirth or intrauterine distress. Maintaining stability in blood glucose levels is crucial throughout pregnancy, directly impacting the safety of both the mother and the baby.[7-8]

Pregnancy is a distinctive phase for women, marked by the gradual growth of the baby as the pregnancy unfolds. As the fetus matures, its nutritional requirements increase, necessitating essential nutrients like glucose and energy materials from the mother.[9] Placental requirements for fetal development are met through maternal plasma glucose. Notably, pregnant women exhibit a decrease in plasma glucose levels, particularly in fasting conditions, with a reduction reaching 10% as the pregnancy progresses.[10] Concurrently, the heightened maternal intake of glucose and other energy substances contributes to increased glomerular filtration rate and renal plasma flow.[11] Despite these changes, the glucose reabsorption rate of renal tubules remains constant, leading to a proportional increase in glucose excretion to some extent.[9-11]

Progesterone and estrogen, present in elevated levels during pregnancy, play a crucial role in enhancing glucose utilization.[13] Therefore, fasting blood glucose examination results in pregnant women tend to be lower. However, this hormonal interplay also introduces the risk of ketoacidosis and hypoglycemia in pregnant women. As pregnancy progresses into the second and third trimesters, the body's production of anti-insulin-like substances increases.[14] This condition leads to a decline in insulin sensitivity, necessitating an elevated demand for insulin to maintain normal blood glucose levels. For pregnant women with abnormal insulin secretion, this scenario increases the likelihood of developing diabetic complications, ultimately posing a threat to both maternal and infant health.[7]

In clinical practice, the primary priority for pregnant women diagnosed with diabetes during pregnancy is the prompt control of their blood glucose levels.[14] This immediate intervention aims to minimize potential harm to both the mother and child. Recognizing the unique circumstances of pregnancy, many scholars advocate for a conservative approach to the treatment of gestational diabetes.[14-15] It involves implementing strategies such as exercise and dietary control to achieve the objective of lowering blood sugar levels associated with gestational diabetes. However, in practical terms, it is essential to balance these measures with the nutritional needs required by the pregnant woman's body to support fetal development adequately.[16]

Balancing the nutritional needs of patients with gestational diabetes mellitus poses a challenge when considering conservative treatment strategies aimed at controlling blood glucose levels. Addressing this challenge is essential to seek a balanced and harmonious approach that addresses both concerns effectively.[17] Recognizing the underlying causes of diabetic lesions in gestational diabetes mellitus patients, a cautious approach involves the administration of a specified dose of insulin. This insulin injection aims to promote glycemic decomposition, effectively lowering blood glucose levels.[18]

While the conventional use of insulin in gestational diabetes treatment yields favorable results in blood sugar control, it is crucial to acknowledge that in cases of prolonged high blood sugar, changes in inflammation and hormone levels may occur in pregnant women. Hence, relying solely on insulin might not constitute the optimal treatment plan. A comprehensive and tailored approach is essential for effective management.[19]

In addition to addressing hypoglycemia, it's pivotal to proactively prevent cardiovascular diseases to safeguard the kidney and liver functions of pregnant women with gestational diabetes mellitus. Considering this comprehensive approach, our study advocates for the use of metformin as a treatment strategy.[8] Metformin stands as a primary pharmacological choice for diabetes treatment, functioning as an oral hypoglycemic drug. Upon oral administration, its effectiveness peaks within two hours, and notably, it does not bind with plasma proteins. The drug is excreted through the patient's urine, with a duration of action lasting up to 8 hours. Common adverse reactions following metformin use encompass nausea, vomiting, dyspepsia, diarrhea, and headache.[17-18]

Before initiating metformin treatment, it is imperative to exclude patients with a known allergy to metformin carefully. Metformin primarily acts upon the muscle cells, pancreatic cells, and liver cells within the patient's body. It significantly influences the glucose processing capacity of these cells, inhibiting glucose formation within the liver and enhancing peripheral tissue insulin sensitivity. This results in improved

glucose utilization in bone tissues. Metformin's multifaceted effects also include the inhibition of glucagon secretion by pancreatic cells, ultimately achieving the goal of reducing patients' blood glucose levels. Importantly, metformin does not induce hypoglycemia, contribute to obesity, and exhibit noteworthy anti-inflammatory and anti-tumor effects. Thus, metformin stands out as an effective and well-rounded treatment option for gestational diabetes.[9]

In this study, we conducted a comprehensive comparison of the clinical effects between the insulin regimen and the metformin treatment regimen for gestational diabetes mellitus. The findings are as follows: Before treatment initiation, the 2-hour postprandial blood glucose level was (13.22±2.15) mmol/L, fasting blood glucose level stood at (8.46±1.23) mmol/L, and the glycosylated hemoglobin level was (8.99±1.23)%. In the control group, the 2-hour postprandial blood glucose level measured (13.28±2.11) mmol/L, the fasting blood glucose level displayed (8.47±1.21) mmol/L, and the glycosylated hemoglobin level was (8.97±1.21)%. After treatment, the postprandial 2-hour blood glucose level dropped to (8.56±1.12) mmol/L, fasting blood glucose level decreased to (4.85±1.31) mmol/L, and the glycosylated hemoglobin level notably reduced to (5.63±1.01)%.

In the control group, the 2-hour postprandial blood glucose level measured (10.62±1.32) mmol/L, the fasting blood glucose level was (6.24±1.23) mmol/L, and the glycosylated hemoglobin level was (6.97±1.12)%. This result indicates that both treatment regimens effectively lower blood glucose levels, with metformin demonstrating superior efficacy in improving blood glucose compared to the control group.

Moreover, before treatment initiation, the study group exhibited IL-8, TNF-α, and IL-1β levels of (353.54±39.52) pg/ml, (29.65±5.12) ng/L, and (19.16±4.23) ng/L, respectively. In the control group, the pre-treatment levels of IL-8, TNF-α, and IL-1β were recorded as (353.57±39.54) pg/ml, (29.68±5.16) ng/L, and (19.12±4.21) ng/L, respectively. Following treatment, a significant reduction was observed in the levels of these inflammatory markers to (195.52±20.85) pg/ml, (12.43±2.12) ng/L, and (7.52±2.23) ng/L, respectively. In comparison, the control group exhibited pre-treatment levels of (236.72±28.53) pg/ml, (19.21±3.21) ng/L, and (12.36±2.68) ng/L for IL-8, TNF-α, and IL-1β. These results highlight the similarity in the baseline levels of inflammatory markers between the two groups before treatment.

After the intervention, there was a notable improvement in the levels of IL-8, TNF-α, and IL-1β in both groups when compared to the pre-treatment values. The study group exhibited a more pronounced enhancement in these inflammatory markers compared to the control group. In the pre-treatment phase, the levels of CysC and Hcy were recorded as (1.24±0.22) mg/L and (13.72±3.52) μmol/L in the study group, and (1.25±0.23) mg/L and (13.76±3.54) μmol/L in the control group.

After the intervention, the levels of CysC and Hcy exhibited notable improvements. In the study group, the post-treatment levels were recorded as (0.61±0.12) mg/L and (7.38±1.52) μmol/L, while in the control group, these levels were (0.88±0.19) mg/L and (9.58±1.76) μmol/L. These results suggest that the baseline levels of CysC and Hcy were comparable between the two groups before treatment. However, after the intervention, both groups showed significant enhancements, with the study group demonstrating a superior improvement compared to the control group.

In the study group, there was one reported case of hypertension and premature delivery, resulting in a defect rate of 4.17% (2/48). Conversely, the control group experienced four cases of hypertension, three cases of premature delivery, and one case of preeclampsia, contributing to a defect rate of 4.17% (8/48). Additionally, the study group recorded one case each of hypoglycemia and macrosomia, accounting for a defect rate of 4.17% (2/48). In contrast, the control group encountered two cases of respiratory distress syndrome, three cases of hypoglycemia, and three cases of macrosomia, yielding a defect rate of 4.17% (8/48).

These findings indicate a lower incidence of adverse outcomes in the study group compared to the control group. The comparison of two treatment approaches for gestational diabetes reveals that both insulin and metformin effectively lower blood sugar levels. However, metformin demonstrates superior efficacy in reducing adverse outcomes. Moreover, the metformin plan exhibits a more favorable control over inflammation and hormone levels, offering enhanced protection for both pregnant women and fetuses. Consequently, metformin emerges as a more beneficial treatment option.[10]

The study results underscore the efficacy of both insulin and metformin in effectively reducing blood sugar levels among patients with gestational diabetes. Notably, metformin exhibited superior outcomes in mitigating adverse events compared to the insulin regimen. The data suggest that metformin not only contributes to better glycemic control but also demonstrates a more favorable impact on inflammation and hormone levels, crucial factors in gestational diabetes management. These outcomes emphasize the potential of metformin as a promising treatment option, offering enhanced protection for both pregnant women and their fetuses. These findings contribute valuable insights into optimizing treatment strategies for gestational diabetes mellitus.

Study Limitations

This study has certain limitations to consider. The sample size may not fully represent the broader population of pregnant women with gestational diabetes. The study's duration might not capture long-term effects, and further research with extended follow-up is needed. The absence of a placebo group limits the ability to isolate specific treatment effects. Patient adherence variations could influence outcomes. The focus on specific clinical parameters excludes broader maternal and neonatal outcomes. Acknowledging these limitations is crucial for interpreting the results accurately and highlights areas for future research.

CONCLUSION

In conclusion, this study highlights the noteworthy clinical impact of metformin therapy in managing gestational diabetes mellitus. The comparative analysis with insulin therapy reveals superior outcomes in terms of blood glucose control, inflammation mitigation, and hormone level regulation. Additionally, metformin demonstrates favorable results in maternal and infant outcomes. These findings advocate for the consideration and recommendation of metformin as a viable therapeutic option for patients dealing with gestational diabetes mellitus.

ACKNOWLEDGMENT

None

CONFLICTS OF INTEREST

The authors report no conflict of interest.

AVAILABILITY OF DATA AND MATERIALS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

FUNDING

No funding.

REFERENCES

1. Bellani S, Bartolotta A, Agresti A, et al. Solution-processed two-dimensional materials for next-generation photovoltaics. *Chem Soc Rev*.2021;50(21):11870-11965. Published 2021 Nov 1. doi:10.1039/d1cs00106j
2. Tertti K, Laine K, Ekblad U, Rinne V, Rönnemaa T. The degree of fetal metformin exposure does not influence fetal outcome in gestational diabetes mellitus. *Acta Diabetol*. 2014;51(5):731-738. doi:10.1007/s00592-014-0570-6
3. Farrar D, Simmonds M, Bryant M, et al. Hyperglycaemia and risk of adverse perinatal outcomes: systematic review and meta-analysis. *BMJ*. 2016;354:i4694. Published 2016 Sep 13. doi:10.1136/bmj.i4694
4. Mills JL, Knopp RH, Simpson JL, et al. Lack of relation of increased malformation rates in infants of diabetic mothers to glycemic control during organogenesis. *N Engl J Med*.1988;318(11):671-676.doi:10.1056/NEJM198803173181104
5. Diabetes Prevention Program Research Group, Knowler WC, Fowler SE, et al. 10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study [published correction appears in Lancet. 2009 Dec 19;374(9707):2054]. *Lancet*. 2009;374(9702):1677-1686. doi:10.1016/S0140-6736(09)61457-4
6. Feig DS, Donovan LE, Zinman B, et al. Metformin in women with type 2 diabetes in pregnancy (MiTy): a multicentre, international, randomised, placebo-controlled trial [published correction appears in Lancet Diabetes Endocrinol. 2020 Nov;8(11):e6]. *Lancet Diabetes Endocrinol*. 2020;8(10):834-844. doi:10.1016/S2213-8587(20)30310-7
7. Feig DS, Donovan LE, Zinman B, et al. Metformin in women with type 2 diabetes in pregnancy (MiTy): a multicentre, international, randomised, placebo-controlled trial [published correction appears in Lancet Diabetes Endocrinol. 2020 Nov;8(11):e6]. *Lancet Diabetes Endocrinol*. 2020;8(10):834-844.doi:10.1016/S2213-8587(20)30310-7
8. Yuan LJ, Qin Y, Wang L, et al. Capsaicin-containing chili improved postprandial hyperglycemia, hyperinsulinemia, and fasting lipid disorders in women with gestational diabetes mellitus and lowered the incidence of large-for-gestational-age newborns. *Clin Nutr*. 2016;35(2):388-393. doi:10.1016/j.clnu.2015.02.011
9. Rowan JA, Hague WM, Gao W, Battin MR, Moore MP; MiG Trial Investigators. Metformin versus insulin for the treatment of gestational diabetes [published correction appears in N Engl J Med. 2008 Jul 3;359(1):106]. *N Engl J Med*. 2008;358(19):2003-2015. doi:10.1056/NEJMoa0707193
10. Crowther CA, Samuel D, McCowan LME, et al. Lower versus Higher Glycemic Criteria for Diagnosis of Gestational Diabetes. *N Engl J Med*. 2022;387(7):587-598. doi:10.1056/NEJMoa2204091