https://doi.org/10.32441/kjps.06.01.p3

Al-Kitab Journal for Pure Sciences
ISSN: 2617-1260 (print), 2617-8141(online)
www.kjps.isnra.org

Comparative Study between Metformin and Insulin in Controlling uncomplicated Gestational Diabetes Mellitus

Enas Yahya Ibraheem*, Israa Hashim Abid Al-Karim

Tikrit University, Iraq

*Corresponding Author: enasaltemem@gmail.com

Citation: Ibraheem EY, Abid Al-Karim IH. Comparative Study between Metformin and Insulin in Controlling uncomplicated Gestational Diabetes Mellitus. *Al-Kitab Pure Sci KJPS*. 2022; 6(1): 30-41. https://doi.org/10.32441/kjps.06.01.p3.

Keywords
Metformin, Insulin, GDM.

Article History
Received 20 Feb. 2022
Accepted 12 July 2022
Available online 30 Aug 2022

Abstract:

Gestational diabetes always accompanies an increased maternal and neonatal risk. Insulin is the standard therapy but causes multiple complications. Metformin has less complications. This study aims to assess the efficacy of metformin in controlling maternal blood glucose level compared to insulin in women with gestational diabetes.

A randomized controlled trial conducted in the obstetric department in Salah Al-Deen general Hospital during the period from 1st February - 31st July 2022. Total sample of 100 pregnant women suffered from gestational diabetes at (24-28week) gestational age were recruited randomly. The patients were divided into two groups: 1-Metformin group (50 patients). 2-Insulin Group (50 patients). Fasting and post prandial blood glucose levels 2 h after breakfast were done at each visit and HbAlc each trimester. Follow up was continued till delivery to evaluate the pregnancy outcome .

The mean HbAlc was significantly higher among Insulin group (5.8± 0.5) than in Metformin group (5.4 ± 0.8). Preeclampsia was lower among Metformin group (14%) than Insulin group (19.6%). hypoglycemia episode was significantly lower among Metformin group (14%) than Insulin group (41.3%), Caesarean delivery was higher among Insulin group (58.7%) than Metformin group (37.2%). The mean birth weight was significantly higher among Insulin group (3761.4±470) than Metformin group (3540.9±338). Prematurity was found among (8.7%) of the Insulin group in comparison to (4.7%) of the Metformin group. Prematurity was non significantly higher among Insulin group (8.7%) than Metformin group (4.7%).

Metformin is effective and safe in the glycemic control of gestational diabetes, with better maternal and neonatal outcomes.

Keywords: Metformin, Insulin, GDM.

دراسة مقارنة بين الميتفورمين والأنسولين في السيطرة على الحمل السكري غير المعقدة

إيناس يحيى إبراهيم*، إسراء هاشم عبد الكريم

جامعة تكريت، العراق

* enasaltemem@gmail.com

الخلاصة:

يصاحب سكري الحمل دائمًا زيادة أخطار الأمهات والمواليد. الأنسولين هو العلاج القياسي ، ولكنه يسبب مضاعفات متعددة. الميتفورمين له مضاعفات أقل. تهدف هذه الدراسة إلى تقييم فعالية الميتفورمين في السيطرة على مستوى السكر في الدم لدى الأمهات مقارنة بالأنسولين لدى النساء المصابات بسكري الحمل.

أجريت دراسة سريريه منضبطة أجريت في قسم النسائية والتوليد بمستشفى صلاح الدين العام خلال الفترة من ١ فبراير - ٣١ يوليو ٢٠٢٢. تم تجنيد ما مجموعه ١٠٠ حامل مصابة بسكري الحمل بعمر الحمل (٢٤-٢٨ أسبوعًا). تم تقسيم المرضى عشوائياً إلى مجموعتين: ١ - مجموعة الميتفورمين (٥٠ مريضاً. ٢ - مجموعة الأنسولين (٥٠ مريضاً). تم إجراء فحص نسبه السكر في الدم بعد الصيام وبعد تناول الطعام بساعتين بعد الإفطار في كل زيارة وقياس HBA1C كل ثلاثة أشهر. استمرت المتابعة حتى الولادة لتقييم نتيجة الحمل.

كان متوسط HBA1C أعلى بشكل ملحوظ بين مجموعة الأنسولين (٥,٨ ± ٠,٥) منه في مجموعة METFORMIN (٥,٤ ± ٠,٨). كانت مقدمات الارتعاج أقل بين مجموعة الميتفورمين (١٤٪) من مجموعة الأنسولين (١٩,٦٪). كانت نوبة نقص السكر في الدم أقل بشكل ملحوظ بين مجموعة الميتفورمين (١٤٪) من مجموعة الأنسولين (٤١,٣٪) ، وكانت الولادة القيصرية أعلى بين مجموعة الأنسولين (٥٨,٧٪) من مجموعة الميتفورمين (٣٧,٢٪). كان متوسط وزن الولادة أعلى بشكل ملحوظ بين

مجموعة الأنسولين (٣٧٦١,٤ ± ٤٧٠) من مجموعة الميتفورمين (٣٥٤٠,٩ ± ٣٣٨). وُجدت الخداج عند (٨,٧٪) من مجموعة الأنسولين مقابل (٤,٧٪) في مجموعة الميتفورمين. كانت الخداج غير أعلى معنويا بين مجموعة الأنسولين (٨,٧٪) من مجموعة الميتفورمين (٤,٧٪).

الميتفورمين فعال وآمن في السيطرة على نسبة السكر في الدم لمرض سكري الحمل ، مع نتائج أفضل للأمهات والأطفال حديثي الولادة.

الكلمات المفتاحية: الميتفورمين والأنسولين في سكري الحمل ، مقارنة الميتفورمين والأنسولين في سكري الحمل.

1. INTRODUCTION:

Gestational Diabetes Mellitus (GDM) is said to occur late in pregnancy as a transient condition with less severe hyperglycemia [1], differing from diabetes in pregnancy (DIP) where diabetes overt in pregnancy and likely to continue after birth. However, recent literature suggests there may also be an entity related to early-onset GDM which may be distinct from DIP and a separate subset of hyperglycemia in Pregnancy (HIP) [2], as GDM typically appears in the second or third trimester. GDM exhibits a large proportion of HIP, with estimates that it represents 75–90% of all HIP cases [3].Insulin is the standard therapy for GDM management in cases refractory to nutrition therapy and exercise. Insulin therapy can be difficult for pregnant women due to multiple injection requirements, risk of hypoglycemia, and weight gain. In addition, hypoglycemia occurs in 70% of women who use insulin in their pregnancy. [4] Metformin is a type of oral hypoglycemic medications called Biguanides. Metformin decreases hepatic gluconeogenesis, improves peripheral and hepatic sensitivity to insulin and does not induce hypoglycemia or maternal weight gain. However, as Metformin crosses the placenta and the long-term effects in the offspring are unknown. There are more than 10 studies assessing Metformin safety and efficacy. Globally, the results have been favorable to Metformin. Compared to women taking insulin, those under Metformin have no difference in maternal glycemic control, congenital abnormalities, macrosomia, rates of neonatal hypoglycemia or other maternal or neonatal adverse outcomes. [5] This study aims to assess the efficacy of metformin in controlling maternal blood glucose level compared to insulin in women with GDM.

3. Patients and Methods

This study is a Randomized controlled trial was conducted in obstetric department in Salah Al-Deen general Hospital during the period from 1st February to the 31st of July 2022. Total

of 100 pregnant patients that diagnosed with GDM with gestational age (24-28week) were randomly selected from the outpatient clinic and divided for two groups randomly into: group metformin (50 patients), and insulin group (50 patients). Inclusion criteria were patients diagnosed to have GDM were treatment initiated before 34 weeks of gestation. Exclusion Criteria were essential hypertension, preeclampsia, Intra uterine growth retardation, Abnormal glucose tolerance before pregnancy, unbalanced chronic disease, twin pregnancy, and treatment initiated before 12 weeks or after 34 weeks of gestation. Data Collection done through a questionnaire: by direct interview with the pregnant women, taking information about demographic variable, & obstetrical history. Careful general clinical examination including body weight, height, blood pressure and lower limb edema. Maternal body mass index. & Abdominal examination for assessment of estimated fetal weight, fetal movement. Ultrasonography to confirm gestational age, to exclude Intra uterine growth retardation, congenital fetal malformation, and twin pregnancy. Preterm was diagnosed as gestational age at delivery < 37 completed weeks. Laboratory examination: blood samples were collected from the mothers for the diagnosis of GDM which made with at least two out of three elevated glucose levels & FBG. These testes were done for pregnant women with high risk for GDM on booking visit and pregnant women with low risk for GDM were screened at 24-28 weeks. Before intervention patients were advised to take standard nutritional instruction for three meals and four snakes daily.

Metformin Group: Metformin was started at dose of 500 mg and increased up to 1500 mg in 3 divided doses as tolerated until glycemic control was achieved **[6]**. Insulin group: Insulin was prescribed as a combination of short acting and intermediate acting human insulin, twice daily before meals in the morning and in the evening. A 24 h total insulin dose was calculated using 1 units/kg body weight. Two thirds of total dose was given in morning before breakfast and one third at night before dinner **[6]**.

Follow up: Follow up visits will arrange every 2 weeks till 36 weeks then weekly till delivery. All patients were taught self-blood sugar monitoring using home glucose monitors and will advised to maintain written record of blood sugar levels. Fasting and post prandial blood glucose levels 2 h after breakfast were done at each visit and Glycated hemoglobin (HbAlc) each trimester. Primary outcome measure is control of diabetes mellitus; monitored by fasting blood sugar level, two hours postprandial, and HbA1C. Secondary outcome measure is obstetric complications; macrosomia, shoulder dystocia, and rate of cesarean section.

3. Results

Enrollment of 100 pregnant women with gestational diabetes, 11 were lost to follow and 3 of the Metformin group were shifted to insulin management due to irresponsive to metformin and excluded from the study. The droop out rate was 11% lower than the accepted rate <20%, as shown in **Figure 1**.

Most of the patients in both groups insulin group and metformin group were aged (31-40 years), (47.83%), and (48.84%) respectively, this relation was statistically not significant. Most of the patients in both groups' insulin group and metformin group from urban areas, (63.04%), and (62.29%) respectively, this relation was statistically not significant. Most of the patients in insulin group and metformin group were with parity ≥3 (50%), (48.84%), respectively, this relation was statistically not significant .

Positive history of previous GDM found among (23.91%), and (20.93%) among insulin group, and metformin group respectively. Positive family history of diabetes mellitus found among (47.83%), and (53.49%) among insulin group, and metformin group respectively, this relation was statistically not significant. The mean gestational age at diagnosis was (28.3±5.2 week) among insulin group, and (29.5± 4.9 week) among metformin group as shown in **Table 1**.

Most of the patient were obese (BMI ≥30Kg/m 2) among insulin group (47.8%) and metformin group (46.5%), followed by overweight 13(28.3%), and 14(32.6%) respectively as shown in **Table 2**.

The mean systolic blood pressure among insulin group was (115.5±14.3), in comparison with metformin group (117.3±12.4), as shown in **Table 3**. The mean diastolic blood pressure among insulin group was (77.3±9.8), in comparison with metformin group (75.3±10.3), as shown in **Table 3**.

After the end of the treatment the results show that: The mean FBS was higher among insulin group (89.5± 7.2) than in metformin group (87.3± 5.01), this relation was statistically significant as shown in **Table 4**. The mean post prandial blood glucose2 h after breakfast was higher among insulin group (125.5± 5.7) than in metformin group (122.8± 4.1), this relation was statistically significant as shown in **Table 4**. The mean HbAlc was higher among insulin group (5.8± 0.5) than in metformin group (5.4 ± 0.8), this relation was statistically significant as shown in **Table 4**.

Preeclampsia non significantly was lower among metformin group 6(14%) than insulin group (19.6%). hypoglycemia episode was lower among metformin group (14%) than insulin group (41.3%), this relation was statistically significant (P value < 0.05), as shown in **Table 5**. Caesarean delivery was higher among insulin group (58.7%) than metformin group (37.2%), this relation was statistically significant as shown in **Table 5**.

The mean birth weight was higher among group I (3761.4±470) than group M (3540.9±338) this relation was statistically significant as shown in **Table 6**. Prematurity was found among 4(8.7%) of the insulin group in comparison to 2(4.7%) of the metformin group, this relation was statistically non-significant as shown in **Table 6**.

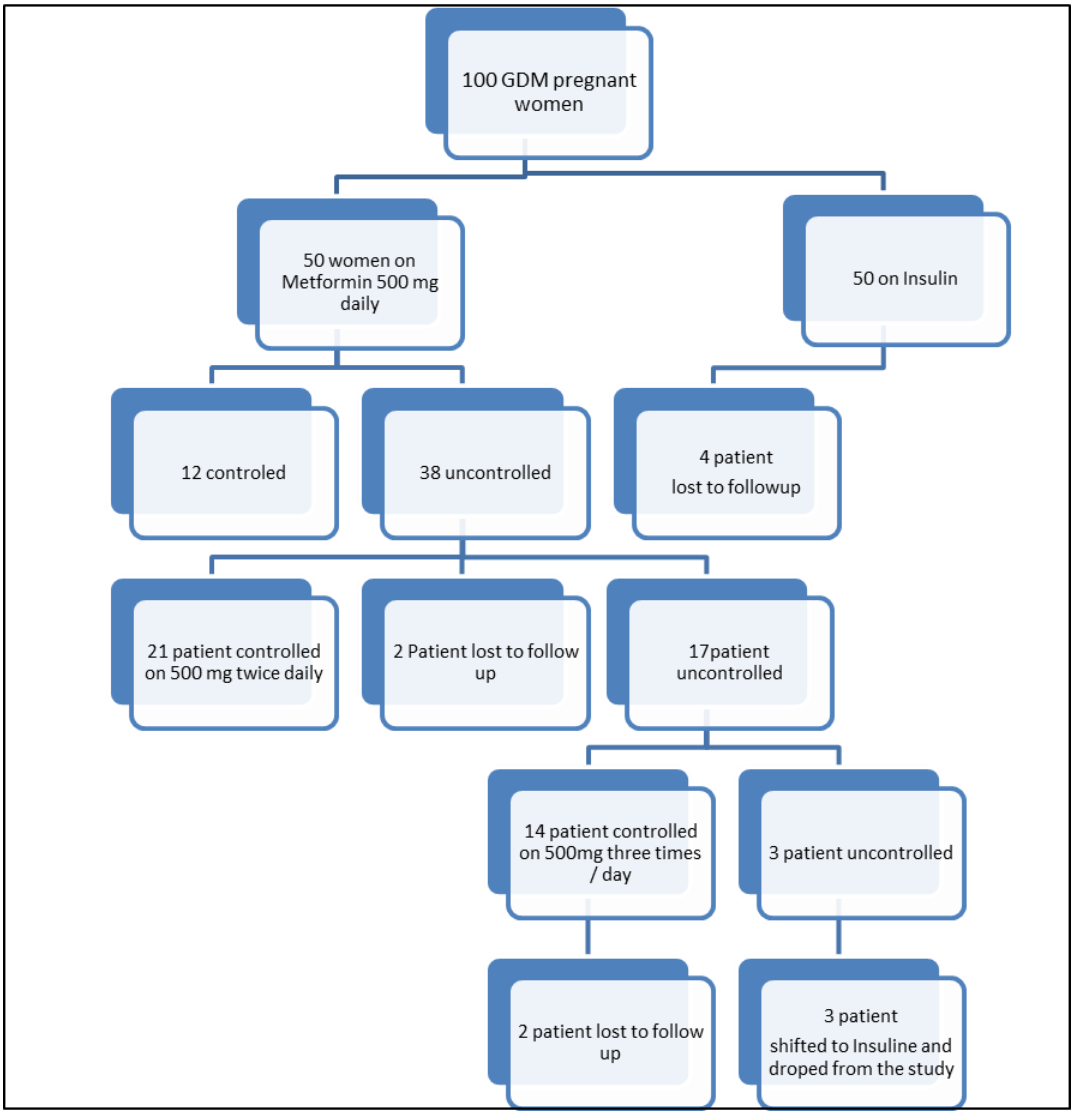

Figure 1. The study participant's flowchart.

Table 1. The general baseline characteristics of the sample.

	Insulin Group (n=46)		**Metformin Group (n=43)**		
Age	Frequency	%	Frequency	%	P value
<20 years	6	13.04	5	11.63	> 0.05 NS
21-30 years	18	39.13	17	39.53	
31- 40 years	22	47.83	21	48.84	
Total	46	100.00	43	100.00	
Urban	29	63.04	27	62.79	
Rural	17	36.96	16	37.21	> 0.05 NS
Parity					
Nulliparous	10	21.74	8	18.60	
1_2	13	28.26	14	32.56	> 0.05 NS
≥3	23	50.00	21	48.84	
Total	46	100.00	43	100.00	
previous GDM					
positive	11	23.91	9	20.93	> 0.05 NS
Negative	35	76.09	34	79.07	
Total	46		43		
DM Family history		0.00		0.00	
Positive	22	47.83	23	53.49	> 0.05 NS
Negative	24	52.17	20	46.51	
Total	46	100.00	43	100.00	
Gestational age at diagnosis of GDM (week)		28.3±5.2	29.5± 4.9		> 0.05 NS

Table 2. the sample distribution according to pre pregnancy BMI

BMI	**Insulin Group**		**Metformin Group**	
	Frequency	%	Frequency	%
Normal (18.5-24.9) Kg/m 2	11	23.9	9	20.9
Overweight (25-29.9) Kg/m 2	13	28.3	14	32.6
Obese (≥30) Kg/m 2	22	47.8	20	46.5
Total	46	100.0	43	100.0

Table 3. The sample distribution according to blood pressure

BP	**Insulin Group**		**Metformin Group M**		**P value**
	Mean	SD	Mean	SD	
Systolic	115.5	14.3	117.3	12.4	>0.05
Diastolic	77.3	9.8	75.3	10.3	>0.05

Table 4. The sample distribution according to blood glucose indices

Blood Glucose Indices	Insulin group		Metformin group		
	Mean	SD	Mean	SD	
FBS (mg/dl)	89.5	7.2	87.3	5.01	<0.05(2.8)
Post prandial blood glucose 2 h after breakfast (mg/dl)	125.5	5.7	122.8	4.1	<0.05(2.8)
HbAlc	5.8	0.5	5.4	0.8	<0.05(2.8)

Table 5. The sample distribution according to maternal outcomes

Maternal outcomes	**Insulin group**		**Metformin group**		**P value**
	Frequency	**%**	**Frequency**	**%**	
Preeclampsia	9	19.6	6	14.0	>0.05 NS
hypoglycemia episode	19	41.3	6	14.0	<0.05 S
mode of delivery					
vaginal delivery	19	41.3	27	62.8	
Caesarean	27	58.7	16	37.2	<0.05 S
Total	46	100	43	100	

Table 6. The sample distribution according to Neonatal outcomes

Neonatal outcomes	**Insulin group**		**Metformin Group**		**P value**
	Frequency	%	Frequency	%	
Birth weight (gr) mean± SD*	3761.4±470		3540.9±338		<0.05 S*
Prematurity	4	8.7	2	4.7	>0.05 NS***

*SD: standard deviation, **S: significant, ***NS: non-significant

4. Discussion

In both groups of the current study, Insulin group and Metformin group most of the patients were aged (31-40 years), (47.83%), and (48.84%) respectively, this goes with Baiee HA et al 2014 [7] who found that the women with gestational diabetes are older (49.3%) aged > 30 years , and with Mdoe MB et al 2021[7] found that maternal age above 35 years associated with GDM. Most of our patients from urban area in both groups; Insulin group (63.04%) and Metformin group (62.29%), this goes with Baiee HA et al 2014 [7] who found that most cases are living in urban regions. Mdoe MB et al 2021[8] found that most of GDM women were from urban areas (63%).

In current study the mean FBS was significantly higher among Insulin group (89.5± 7.2) than in Metformin group (87.3± 5.01). This goes with Aboud AL Hayani, and Nasir A 2020, [9] Found that patients on metformin treatment had significantly lower glucose levels

(78.7±3.2) than insulin treated group (86.92±3.31). Ghomian N et al 2019 [10] found that fasting plasma glucose (FPG) was controlled well by both groups' metformin treatment (91.22 ± 4.37) and insulin treatment (92.21 ± 4.41) without any significant difference. Simeonova-Krstevska S 2018 [11] found that the mean FPG was statistically significantly lower in metformin group (5.3±0.7 mmol/l) than in insulin group (5.8± 1.4 mmol/l). The mean post prandial blood glucose 2 h after breakfast was significantly higher among insulin group (125.5± 5.7) than in metformin group (122.8± 4.1), this goes with Ghomian N et al 2019 [10] found that postprandial glycemia control an metformin treated group (119.38 ± 4.03) was lower than among insulin treated group (118.99 ± 6.24), and with Simeonova-Krstevska S 2018 [11] found that the mean postprandial glycaemia was statistically significantly lower in metformin group (7.0 ± 1.2 mmol/l) than in insulin group (7.9 ± 1.9 mmol/l).

In current study the mean HbAlc was significantly higher among insulin group (5.8± 0.5) than in metformin group (5.4 ± 0.8). this supported by the findings of Sarwat A et al 2022 [12] found that maternal HbA1c levels before birth were 6.1±1.1 in metformin group and 6.0±1.2 in insulin group, and with Simeonova-Krstevska S 2018 [11] found that the mean glycosylated hemoglobin (HbA1c) at 37 gestation week was significantly lower in metformin groups (5.3±0.7) than in insulin group (6.2±1.8). Preeclampsia non significantly was lower among metformin group (14%) than insulin group (19.6%). This supported by what found by Kalafat ER et al 2018 [13] found that metformin use was associated with a reduced risk of pregnancy-induced hypertension when compared with insulin and a non-significantly reduced risk of pre-eclampsia. Hypoglycemia episode was significantly lower among metformin group (14%) than insulin group (41.3%). This goes with Picón-César, M.J et al 2021 [14] found that insulin treated group had more hypoglycemic episodes (55%) than the metformin treated group (17.7%). Ruholamin S et al 2014 [15] described only 2 women having hypoglycemia on insulin and none on metformin, and Ashoush et al 2016 [16] published a non-significant difference for maternal hypoglycemic episodes. Caesarean delivery was significantly higher among insulin group (58.7%) than metformin group (37.2%). This goes with Picón-César, M.J et al 2021 [14] found that cesarean deliveries (27.6% [metformin] vs 52.6% [insulin.]). Aboud AL Hayani, and Nasir A 2020 [9] found a significant difference between insulin and metformin groups as regards mode of delivery as insulin group (59.4%) has higher percentage than metformin groups (40-57.1%) according to metformin dose in cesarean delivery.

A meta-analysis done by Guo L et al 2019 [17] published a lower incidence of labor induction and a tendency to fewer elective cesarean deliveries for metformin treatment. The

mean birth weight was significantly higher among group insulin (3761.4±470) than metformin group M (3540.9±338). This goes with Aboud AL Hayani, and Nasir A 2020 **[9]** found that there were statistically significant differences between insulin group (4.1±0.12 kg) and metformin sub-groups patients as regards birth weight. Wang X et al 2021**[18]** and Jiang YF et al 2015 **[19]** found that metformin was with lower neonatal birth weight, in which the results were the same as a previous study. Ghomian N et al 2019 **[15]** found no different between metformin group (3,450 ± 548), insulin group (3,544 ± 57) regarding birth weight. Zhou et al 2021 **[20]** suggested that the level of triglyceride in maternal blood was positively correlated with neonatal birth weight. Metformin is also confirmed to reduce the level of triglyceride in non-obese type 2 DM patients, as a result, the potential mechanism for metformin to reduce neonatal birth weight is improved maternal lipid metabolism **[20].**

5. Conclusions

Metformin is effective and safe in the glycemic control of GDM, Metformin treated women had better maternal and neonatal outcomes, less hypoglycemic attacks and less preeclampsia, macrosomia and preterm labour. Larger multicenter studies are recommended to establish the long-term outcomes.

6. References

[1] American Diabetes Association (ADA). Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. Diabetes Care (2020); 43(Supplement 1): S14–S31.

[2] Immanuel J, Simmons D. Screening and treatment for early-onset gestational diabetes mellitus: a systematic review and meta-analysis. Curr Diab Rep. 2017;17(11). https://doi.org/10.1007/s11892-017-0943-7.

[3] International Diabetes Federation. IDF Diabetes Atlas. Brussels, Belgium: International Diabetes Federation 2017.

[4] Catherine A, Elie S and Julie M (2014): Gestational Diabetes Mellitus Identification Based on SelfMonitoring of Blood Glucose. Canadian Diabetes Association, 5:1-9. 3.

[5] Kristi WK, Dana GC and Allison M: A review of current, treatment strategies for gestational diabetes mellitus. Drugs Context(2015), 4:212-222. 5.

[6] Jahanara A, Nasam K and Sanower AH. Metformin versus insulin treatment in gestational diabetes in pregnancy in a developing country. A randomized control trial. Diabetes Res Clin Pract (2014); 107(2):290-9.

[7] Baiee HA, Fliah M, Abd Alkareem D, Hamid S, Salim A. Factors Associated with Gestational Diabetes Mellitus in Babylon, Iraq During The Year 2014. Medical Journal of Babylon. 2016;13(1):24-31.

[8] Mdoe MB, Kibusi SM, Munyogwa MJ, Ernest AI. Prevalence and predictors of gestational diabetes mellitus among pregnant women attending antenatal clinic in Dodoma region, Tanzania: an analytical cross-sectional study. BMJ Nutrition, Prevention & Health. 2021;4(1):69.

[9] Aboud AL Hayani, NASIR A. Metformin versus Insulin in Treatment of Gestational Diabetes. The Medical Journal of Cairo University. 2020 Sep 1;88(September):1967-74.

[10] Ghomian N, Vahed SH, Firouz S, Yaghoubi MA, Mohebbi M, Sahebkar A. The efficacy of metformin compared with insulin in regulating blood glucose levels during gestational diabetes mellitus: a randomized clinical trial. Journal of cellular physiology. 2019 Apr;234(4):4695-701.

[11] Simeonova-Krstevska S, Bogoev M, Bogoeva K, Zisovska E, Samardziski I, Velkoska-Nakova V, Livrinova V, Todorovska I, Sima A, Blazevska-Siljanoska V. Maternal and neonatal outcomes in pregnant women with gestational diabetes mellitus treated with diet, metformin or insulin. Open access Macedonian journal of medical sciences. 2018 May 20;6(5):803

[12] Sarwat A, Perveen N, Saleem A, Rehman F, Zafar I, Iftikhar G. Comparison of Efficacy of Metformin and Insulin in management of Gestational Diabetes. An experience in Social Security Teaching Hospital, Ferozepur Road Lahore. Pakistan Journal of Medical & Health Sciences. 2022 Jun 1;16(05):242-6.

[13] Kalafat ER, Sukur YE, Abdi A, Thilaganathan B, Khalil A. Metformin for prevention of hypertensive disorders of pregnancy in women with gestational diabetes or obesity: systematic review and meta-analysis of randomized trials. Ultrasound in Obstetrics & Gynecology. 2018 Dec;52(6):706-14.

[14] Picón-César, M.J., Molina-Vega, M., Suárez-Arana, M., González-Mesa, E., Sola-Moyano, A.P., Roldan-López, R., Romero-Narbona, F., Olveira, G., Tinahones, F.J. and González-Romero, S.,. Metformin for gestational diabetes study: metformin vs insulin in gestational diabetes: glycemic control and obstetrical and perinatal outcomes: randomized prospective trial. American Journal of Obstetrics and Gynecology2021,; 225(5):517-e1.

[15] Ruholamin S, Eshaghian S, Allame Z. Neonatal outcomes in women with gestational diabetes mellitus treated with metformin in compare with insulin: a randomized clinical trial. J Res Med Sci 2014;19:970–5

[16] Ashoush S, El-Said M, Fathi H, Abdelnaby M. Identification of metformin poor responders, requiring supplemental insulin, during randomization of metformin versus insulin for the control of gestational diabetes mellitus. J Obstet Gynaecol Res 2016;42:640–7

[17] Guo L, Ma J, Tang J, Hu D, Zhang W, Zhao X. Comparative Efficacy and Safety of Metformin, Glyburide, and Insulin in Treating Gestational Diabetes Mellitus: A Meta-Analysis. J Diabetes Res 2019;2019: 9804708

[18] Wang X, Liu W, Chen H, Chen Q. Comparison of insulin, metformin, and glyburide on perinatal complications of gestational diabetes mellitus: a systematic review and meta-analysis. Gynecologic and Obstetric Investigation. 2021;86(3):218-30

[19] 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(5):

2071

[20] Zhou J, Bai J, Guo Y, Fu L, Xing J. Higher levels of triglyceride, fatty acid translocase, and toll-like receptor 4 and lower level of HDL-C in pregnant women with GDM and their close correlation with neonatal weight. Gynecologic and Obstetric Investigation. 2021;86(1):48-54.