IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Research Article
February 2024 Vol.:30, Issue:2

Comparative Study of Antenatal Management in Gestational Diabetes Mellitus with Metformin versus Insulin versus Combination: A Prospective Cohort Study

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Submitted: 19 January 2024
Accepted: 24 January 2024
Published: 29 February 2024

Keywords: Demographic data, Follow-up, Comparison, Metformin, Insulin, subjects

ABSTRACT

Background: Gestational Diabetes mellitus is the most encountered metabolic disorder in obstetrics and remains a major cause of maternal and Fetal morbidity. **Aim:** The present study is aimed to determine the safety and efficacy of metformin versus insulin versus combination in GDM. **Methodology:** A prospective cohort study was carried out in Department of obstetrics and Gynecology including 100 patients based on screening. **Results:** On reviewing data in 100 subjects it was found that most of subjects fall under age group (26-30yrs) with 43% (25.89±4.54), and with normal BMI 54%, HbA1c (5.7-6.4%) with 67%subjects, by comparing FBS and RBS levels before initiation of therapy with follow up was found that Metformin, Insulin (P-value<0.00001) for both FBS and RBS, Combination group with FBS (P-value<0.00001) RBS (0.000123), ADRs are observed in few subjects **Conclusion:** Based on findings Metformin, Insulin and Combination groups are equally effective in controlling glycemic levels in GDM. This study concluded that Metformin is an equally effective and safe alternative to Insulin for women with GDM.

INTRODUCTION:

Gestational Diabetes is the most encountered metabolic disorder in obstetrics in which Human Placental Lactogen a Harmon made by the placenta prevents body from using insulin Effectively results in a build-up of glucose in the blood instead of being absorbed by cells and remain a major cause of maternal and Fetal morbidity[3]. Etiological factors generally include Obesity, Family history, Polycystic ovary syndrome, Alcohol/Smoking, miscarriage, Hypertension, Hyperlipidemia, Hypothyroidism. [1]Decreased or no physical activity, History of Prediabetes, History of Miscarriage or Stillbirth, History of previous delivery with child >4.1 kgs weight, Age>30 years, HbA1C> 5.7 %, Unexplained Perinatal loss, Presence of polyhydramnios, Persistent Glycosuria, Smoking, History of Macrosomia can be added as Risk factors a part from etiological factors[1] ·Most of people presented with symptoms like dry mouth, constipation, fatigue, thrush[6]. GDM is commonly diagnosed with 75gm Oral glucose tolerance test (OGTT) if the FBS >26mg/dl and 2hour post meal blood sugar is>140 mg/dl is considered positive for GDM according to WHO. For this Indication, Metformin and Gliburide are oral hypoglycemics commonly recommended[2]and Insulin is commonly prescribed by physicians. GDM results in maternal complications like Preeclampsia, Neuropathy, Nephropathy, Retinopathy and Diabetic ketoacidosis[7,8] Fetal complications include miscarriage, growth restriction, macrosomia, metabolic syndrome[11,12]

Metformin is a promising oral medication this is often used in several Nations. It has been demonstrated that Metformin is not less effective than Insulin for Glycemic control in Gestational diabetes Mellitus. In our study, we aimed to compare safety and efficacy of Oral Metformin and subcutaneous Insulin in Gestational Diabetes Mellitus.

METHODS

A prospective cohort follow-up study was carried out in obstetrics and gynaecology department at Government general Hospital(GGH)Guntur between September 2022 to March 2023. The safety and efficacy of oral Metformin subcutaneous Insulin and combination was studied. patients were screened based on inclusion and exclusion criteria and enrolled with an informed consent form. A total of 100 women selected based on screening. The self-designed and validated questionnaire was used to assess safety and efficacy of Metformin versus Insulin versus Combination. Collected data initially from screened patients who are using Metformin 69 subjects, Insulin-15 subjects, Combination-

16 subjects and follow-up was done for every 15 days data upto 3 follow-ups with fasting and random blood sugar levels were tabulated and interpreted using statistical tools-one way ANOVA with p-value(<0.05 p-value considered significant).

Table 1: Common Demographics

Parameter	No of Subjects
Age group	
18-20	15
21-25	28
26-30	43
>30	14
BMI	
<18.5	0
18.5-24.9	54
25-29.9	43
>30	3
Diet	
Veg	8
Non-Veg	10
Mixed	82
Chief Complaints	
Diarrhoea	7
Pedal Edema	18
Weakness	11
Abdominal Pain	8
Decreased Appetite	10
Peripheral Limb Pain	2
Vomiting	18
Nil	53
HbA1c	
<5.7%	9
5.7-6.4%	67
>6.4%	24

Table 2 : Glycemic levels before and after treatment with metformin

Shows Metformin has a significant association in controlling glycemic levels in Gestational Diabetic mellitus patients p-value(<0.00001)

variable	Before treatment	After treatment	P value
FBS	109.87±8.45	81.21±6.56	<0.00001
RBS	142.11±15.76	119.35±10.19	<0.00001

Table 3: Glycemic levels before and after treatment with Insulin

Shows Insulin has a significant association in controlling glycemic levels in Gestational Diabetic mellitus patients p-value(<0.00001)

variable	**Before treatment**	**After treatment**	**P value**
FBS	111.93±16.07	85.06±9.43	<0.00001
RBS	154.84±17.69	126.13±10.51	<0.00001

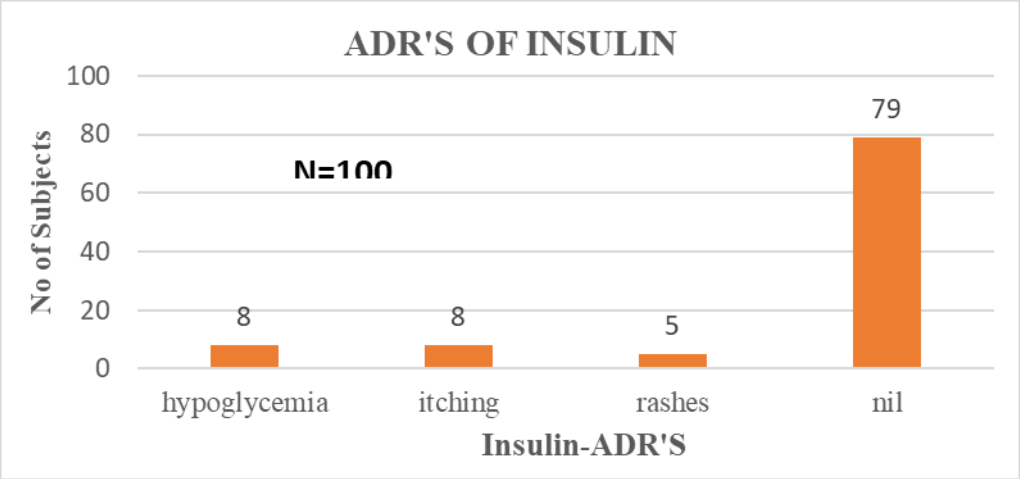
Table 4 : Glycemic levels before and after treatment with Metformin+ Insulin

Shows Metformin and Insulin has a significant association in controlling glycemic levels in Gestational Diabetic mellitus patients p-value FBS(<0.00001), RBS (0.000123)

variable	**Before treatment**	**After treatment**	**P value**
FBS	117.56±6.62	84.12±8.98	<0.00001
RBS	162±35.78	122±8.13	0.000123

Graph 1: ADR of Insulin

It shows that most patients 79(79.00%) have not experienced any Adverse drug effects after taking Insulin but 8(8.00%) experienced Hypoglycaemia 8(8:00%) with Itching 5(5.00%) with Rashes.



Graph 2: ADR of Metformin

shows that most patients 73(73.00%) have not experienced any Adverse drug effects after taking Metformin but 8(8.00%) experienced Diarrhoea few experienced Bloating and Abdominal discomfort 7(7.00%) subjects and 3(3.00%) with decreased appetite and least 2(2.00%) experienced vomiting

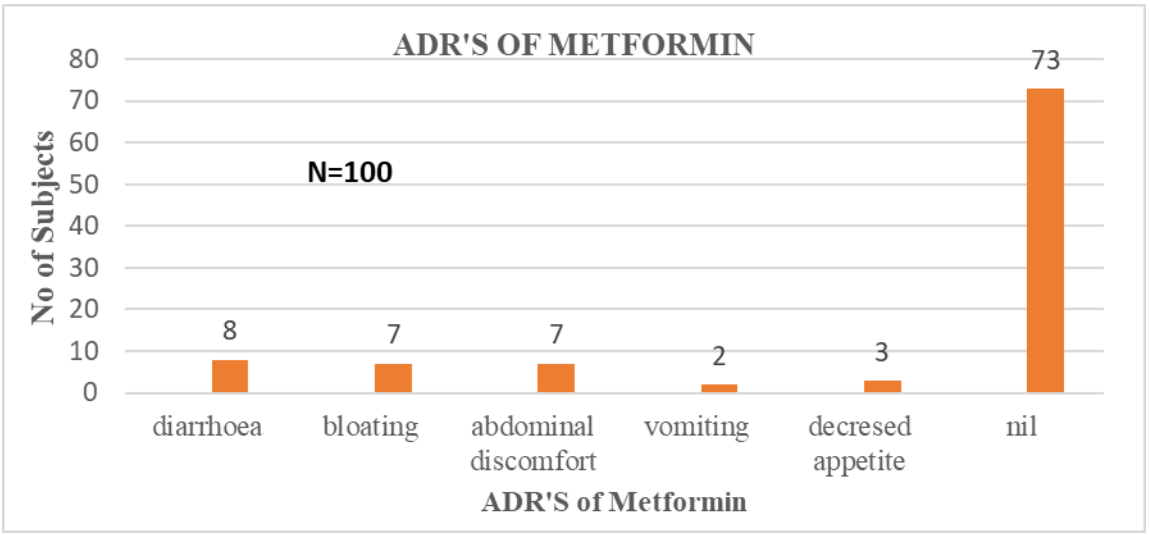


Table 5: Comparison Between Metformin, Insulin, and Combination Groups In Different Parameters

Variable	Metformin N=69	Insulin N=15	Combination N=16	P-value
Age	25.86 ±4.60	26 ±4.97	25.87 ±4.27	0.9949
BMI	24.23 ±2.82	26.70 ±2.70	24.55 ±2.73	0.010365
HbA1c	6.064 ±0.39	6.49 ±0.55	6.44 ±0.44	0.000189

Statistical test used-one way ANOVA

DISCUSSION

Gestational Diabetes Mellitus is one of the most common metabolic disorders observed in pregnancy. Gestational Diabetes Mellitus is associated with maternal complications like preeclampsia, Neuropathy, Nephropathy, Retinopathy, and Ketoacidosis.[11,12]

In a study conducted by Ola Amer Mahmood in 100 pregnant women, the mean age group for Metformin users is 34.20 ± 6.44 years, and for Insulin users mean age group is 31.24 ±6.76. [15]

Titus Beyuo et al in his study with 104 pregnant women observed that the mean age group for Metformin users is 33.51 ±4.67 and for Insulin users is 33.10 ±4.56.[13] A study conducted by Jack Milln et al in 237 subjects the mean age group was 28.5 ± 6.0 years.[14] In our study with 100 subjects, we observed that the mean age group was 25.86 ±4.60 for Metformin users (n=69) 26 ±4.97 for Insulin users (n=15) and 25.87 ±4.27 for both Metformin and Insulin users (n=16) **Table-5**.

In a study conducted by Slagjana Simeonova-Krstevska et al, mean glycosylated Hemoglobin were lower in diet and Metformin than Insulin, in our study mean glycosylated Hemoglobin were lower in the Metformin group (6.064±0.39) than in combination (6.44±0.477) and Insulin group (6.49±0.55) **Table-5.**

In a study conducted by Nayereh Ghomian et.al, Family history, past medical history did not show significant difference between the two groups[16], which is like our study. In our study shows that most of the GDM subjects are mixed diet whose number is 82(82.00%)

followed by 10(10.00%) Nonvegetarians and 8(8.00%) subjects with Pure Vegetarians **Table-1**.

In a study conducted by Ola Amer Mahmood in 100 pregnant women showed that Metformin was better in controlling blood sugar tan compared to Insulin [15]and in a study conducted by Picon-Caesar MJ study concluded that treatment with metformin had a low probability of failure as a standalone therapy, a reduced risk of hypoglycemia episodes, better postprandial glycemic control than insulin for specific meals, and less maternal weight gain. Most prenatal and obstetrical outcomes were comparable between groups[17].

In our study we found that efficacy is equal in treatment groups Metformin, Insulin and Combination (P value-0.00001) which is significant for comparing glycemic levels fasting and random before initiation of therapy and comparing with follow-up glycemic levels in different treatment groups. Whereas treatment with metformin had a reduced risk of hypoglycemia episodes than Insulin users (8%) in **Graph-1.** but few patients using Metformin presented with Gastric problems like Diarrhoea (8%) Bloating (7%) and Abdominal discomfort (7%) in **Graph-2.**

CONCLUSION

In the Present study which is a Prospective cohort follow-up study based on the findings it is concluded that Metformin, Insulin, Mixed are equally effective in controlling glycaemic levels in pregnant women with Gestational Diabetes Mellitus.

However adverse effects are observed with both drugs equally, there is Statistically significant difference present between BMI (P-value=0.010365), HbA1c (P-value=0.000189) levels in Metformin, Insulin, and Mixed groups.

whereas there is no statistically significant difference present between Age (P-value=0.9949) in between 3 groups. Incidence of GDM mostly seen in patients with lower economics and lower educational status. Family history, past medical and medication history had not created any impact in the incidence of GDM.

This study concluded that Metformin is equally effective and safe alternative treatment to Insulin for women with GDM.

ACKNOWLEDGEMENT:

We would like to express our sincere gratitude to Dr. B. Venkateswara Rao MD, DGO,FICOG, Professor and HOD, Department of Obstetrics and Gynecology, Government general Hospital, Guntur and Dr. Y. Gopi pharm.D Assistant Professor, Department of Pharmacy practice, Chalapathi Institute Of Pharmaceutical Sciences(Autonomous) Chalapathi Nagar, Lam, Guntur for their invaluable guidance and insightful discussions throughout the study.

REFERENCES

1.Metzer, B.E, Coustan, D.R.(1998).Summery and recommendations of the fourth International Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee. *Diabetes care*,21 suppl 2, B161-B167.

2.Rickert, M., Caughey, A. B., & Valent, A. M. (2023). Medications for Managing Preexisting and Gestational Diabetes in Pregnancy. *Obstetrics and gynecology clinics of North America, 50(1), 121–136.*

3. Carr DB, Gabbe S(1998) Gestational Diabetes: Detection, Management, and implications. *Clinical Diabetes*;16(1):4-11.

4.McMicking j, Lam AYR, et al. The Continuous Textbook of Women's Medicine SeriesObstetrics module, Glob. libr.*material medical Health and Disorders in Pregnancy*, Vol 8.

5. Fatemeh Nasiri Amiri, PhD,Mahbobeh Faramarzi,PhD, Shabnam Omidvar, PhD(2018).Risk Factors for Gestational Diabetes Mellitus:A Case Cohort Study . *American Journal of Lifestyle Medicine* pg-184-190.

6.Dc Duttas. Textbook of Obstetrics: Including Perinatology and Contraception.8th edition. New Delhi: *Jaypee Brothers Medical Publishers* (P) Ltd; Pg-326-327.

7.Sai Dharshini, S (2017) Metformin, a Convenient Alternative to Insulin in the Management of Gestational Diabetes Mellitus. Master's thesis, PSG Institute of Medical Sciences and Research, Coimbatore.

8.Rowan JA, Hague WM, Gao W, Battin MR, Moore MP (2008) Metformin versus insulin for the treatment of Gestational diabetes. *New England Journal of Medicine* 358(19):20032015.

9.Sopian IL, Shahabudin S, Ahmed MA, Lung LT, Sandai D. (2016) Yeast Infection and Diabetes Mellitus among Pregnant Mothers in Malaysia. *The Malaysian journal of medical sciences.* 2016;23(1):27-34.

10. Solanki A, Sharma M.(2014) Prevalence of Candida infection in pregnant women with and without diabetes. *International Journal of Current Microbiology and Applied Sciences*. 2014;3:605–610.

11.Becerra JE, Khoury MJ, Cordero JF, Erickson JD. (1990) Diabetes Mellitus during pregnancy and the risks for specific birth defects: a population-based case-control study. *Pediatrics*.. 85(1):1-9.

12.De Valk HW, van Nieuwaal NH, Visser GH. (2006) Pregnancy outcome in type 2 diabetes Mellitus: a retrospective analysis from the Netherlands. *Review of Diabetic Studies*. 3(3):13442.

13.Beyuo, T., Obed, S. A., Adjepong-Yamoah, K. K., Bugyei, K. A., Oppong, S. A., & Marfoh, K. (2015). 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*, 10(5), e0125712.

14.Milln, J., Nakabuye, B., Natamba, B.K. (2021) Antenatal management and maternal/fetal outcomes associated with hyperglycemia in pregnancy (HIP) in Uganda; a prospective cohort study. *BMC Pregnancy Childbirth* 21, 386.

15. Mahmood OA. Metformin versus insulin in the management of gestational diabetes mellitus. *Med J Babylon* 2019; 16:346-50.

16.Ghomian, N., Vahed, S. H. M., Firouz, S., Yaghoubi, M. A., Mohebbi, M., & Sahebkar, A. (2019). The efficacy of metformin compared with insulin in regulating blood glucose levels during gestational diabetes mellitus: A randomized clinical trial. *Journal of cellular physiology*, 234(4), 4695–4701.

17.Picón-César MJ, Molina-Vega M, Suárez-Arana M (2021). Metformin for gestational diabetes study: metformin vs insulin in gestational diabetes: glycaemic control and obstetrical and perinatal outcomes: randomized prospective trial. American Journal of Obstetrics and Gynecology;225(5): 517.e1-517.e17.