

# Maternal Weight Gain, BMI and HbA1c Levels In Women With Gestational Diabetes Mellitus Following Treatment With Metformin and Life Style Changes

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## ABSTRACT

**Objective** To find out the maternal outcomes (weight gain, BMI and HbA1c levels) in women with gestational diabetes mellitus treated with metformin along-with life style changes.

**Study design** Quasi study.

**Place & Duration of study** Department of Obstetrics & Gynecology, Sir Syed Hospital and Medical College Karachi, from September 2022 to August 2023.

**Methods** Pregnant women gravida 1- 4, parity 1 - 4, with gestational diabetes mellitus (GDM) were included. Pregnant subjects with excessive weight gain in previous pregnancies, during current pregnancy, predominance of post prandial hyperglycemia, medical disorders like hypothyroidism, liver and kidney diseases, were excluded. GDM was diagnosed using WHO criteria. Women were guided about blood glucose monitoring and dietary intake. Life style changes were also advised. Metformin 500 mg orally was used as first line drug and the dose was titrated up to a maximum of 1500 mg. Data were entered into SPSS 23. Mean comparison of increase in weight, BMI and HbA1c levels from baseline to the 3<sup>rd</sup> trimester was done using Repeated Measure ANOVA. Mann Whitney U test was used to compare the response on weight gain with dosage of metformin. A p-value of < 0.05 were considered statistically significant.

**Results** A total of 100 pregnant women were enrolled from the antenatal clinic. All the patients were in the first trimester of pregnancy. Mean age of the study subjects was 26.2±4.7 years, weight 54±8.4 Kg, BMI 22 ± 2.4 Kg/m<sup>2</sup> and HbA1c 5.9 ± 0.3. All patients were followed till the third trimester. Effect of metformin and life style changes on weight gain, BMI and HbA1c levels during the pregnancy were statistically significant with p<0.05.

**Conclusion** Malformin therapy and lifestyle changes were found safe and effective to control the maternal weight, BMI and HbA1c levels during pregnancy.

**Key words** Gestational diabetes mellitus, Maternal outcome, Pregnancy complications, Diabetes control.

## INTRODUCTION:

Gestational diabetes is defined as any glucose

intolerance which is first recognized during pregnancy. It affects around 14.7% of the population worldwide. Due to increased awareness, detection of GDM by effective screening programs and treatment, the long term consequences of GDM on maternal outcome have improved.<sup>1,2</sup> All pregnant women are screened for diabetes mellitus at two different times in the first trimester of pregnancy by the assessment of fasting plasma glucose levels. If the results are within normal limits then at 24 and 28 weeks of gestation assessment is done by 75gm two hour oral glucose tolerance test (OGTT).

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A diagnosis of GDM is made if fasting blood glucose is  $>92$  mg / dL (in first trimester or 0-hour in OGTT) and hyperglycemia  $>180$  mg / dL or  $153$  mg after 1 and 2-hour OGTT respectively.<sup>3,4</sup>

The treatment of GDM includes life style changes in terms of healthy and balanced diet, regular exercises, weight control and good glycemic control. Metformin plays a major role along with the above changes to attain normal blood sugar levels. It mainly acts by suppressing the hepatic glucose production.<sup>5,6</sup> It is excreted by the kidneys.<sup>7</sup> The impact of metformin on pregnant women is evaluated in number of trials.<sup>8</sup> Tarry-Adkins et al studied the efficacy of metformin in reducing gestational weight gain even in women with a BMI of  $>35$  Kg/m<sup>2</sup>.<sup>9</sup> Other researchers used the combination of health intervention and metformin to obtain the optimal blood glucose levels.<sup>10</sup> In this study we evaluated the results of the metformin as monotherapy along-with the life style changes on maternal weight gain and BMI from booking till term and the glycemic control who had gestational diabetes mellitus.

#### **METHODS:**

**Study design, place & duration:** This quasi study was conducted in the Department of Obstetrics & Gynecology, Sir Syed Medical College & Hospital Karachi, from September 2022 to August 2023.

**Ethical considerations:** The study was approved by the institutional review board (No. CFMP/16/2023 dated 24<sup>th</sup> August 2022). Written informed consent was taken from the patients.

**Inclusion and exclusion criteria:** Women between 20 – 30 years of age, gravida 1 - 4, parity 1 - 4, were included. The exclusion criteria were excessive weight gain in prior pregnancy, during the current pregnancy and predominance of postprandial hyperglycemia. Patients with medical disorders like hypothyroidism and those with hepatic and renal diseases, were also excluded.

**Sample size estimation:** Sample size was not formally calculated. All pregnant women who visited the high-risk antenatal clinic were enrolled. A total of 100 women were the study subjects.

**Study protocol:** Detailed history was taken and physical examination done. Height and weight of the patients were noted at first antenatal or booking visit and BMI calculated. These were assessed at every antenatal visit till the term. GDM was diagnosed using WHO criteria of 2013 by OGTT using 75 gm 2-hour oral glucose tolerance test. The diagnostic

criteria were based upon the fasting glucose level of  $>92$  mg / dL and  $> 153 - 199$  mg / dL after 1 and 2-hours respectively. Other relevant investigations included level of HbA1c.

Patients were encouraged to self-monitor and keep the record of the blood glucose level four times a day (before breakfast, one hour after breakfast, pre-lunch and post dinner). This was done after booking at antenatal clinic for at least one week to assess for the glycemic control. Criteria for glycemic control were as set by WHO and plasma cut off levels were, fasting blood glucose (FBS)  $< 5.3$  mmol/l ( $90-95$  mg / dL), one hour post meal  $< 7.8$  mmol/l ( $140$  mg /dL), and two hours post meal  $< 6.7$  mmol/l ( $120$  mg / dL).

Dietary habits were noted by observing the food intake, once or twice a week. Lifestyle changes included healthy diet (whole fruits and vegetables, moderate amount of lean proteins and healthy fats, moderate amount of whole grains, no soft drinks fruit juices and bakery item. Thirty-minute walk 5 days a week was advised. Metformin was prescribed for glycemic control. Dose was once daily (500mg) to three times daily depending upon the glycemic control.

**Study variables:** Maternal outcomes included the weight gain and BMI, glycemic control, and HA1c level. Other variables studied were the history of diabetes mellitus in the first degree relatives, previous history of intrauterine deaths, GDM diagnosis either first time in the pregnancy or in previous pregnancies, previous big size babies, past history of miscarriages, neonatal deaths and NICU admission.

**Statistical analysis:** Data were stored and analyzed using IBM-SPSS version 23.0. Percentages were reported on demographic variables, routine investigations, past obstetric performance, treatment, and dosage of metformin. Mean with standard deviation were given on age, weight, BMI, HbA1c level, gestational age, FBS, and RBS. Mean comparison of increase in weight, BMI and HbA1c level from baseline to the 3<sup>rd</sup> trimester was done using Repeated Measure ANOVA. Mann Whitney U test was used to compare the response on weight gain with dosage of metformin. A p-value of  $< 0.05$  was considered statistically significant.

#### **RESULTS:**

One hundred pregnant women were enrolled in the study. Forty-three (43%) women were primigravida. The mean age of the study population was  $26.2 \pm 4.7$  years. The mean FBS and RBS

**Table I: Characteristics of The Study Population (n=100)**

Variables		Percentage %	
<b>Gravida</b>	G2	15	
	G3	23	
	G4	19	
	Primigravida	43	
<b>Parity</b>	0	45	
	1	21	
	2	23	
	3	07	
	4	04	
<b>Miscarriage / Abortions (n)</b>	0	78	
	1	17	
	2	05	
<b>Profession</b>			
	Housewife	70	
	Other	30	
<b>Parameters</b>	<b>Mean</b>	<b>±SD</b>	
	Age	26.2	4.7
	Gestational age (weeks) at booking	22.9	2.6
	FBS (mg / dL)	105.7	09.2
	RBS (mg / dL)	152.8	13.3
	HbA1c level	5.9	0.3
	Weight (Kg)	54	8.4
	Height (m)	1.6	0.1
	BMI (Kg/m <sup>2</sup> )	22	2.4

**Table II: Trend of Weight, BMI and HbA1c Level From Baseline to the 3<sup>rd</sup> Trimester**

Parameters	Baseline		2 <sup>nd</sup> Trimester		3 <sup>rd</sup> Trimester		P-value
	Mean	SD	Mean	SD	Mean	SD	
Weight (Kg)	54.2	9.0	60.6	9.1	63.4	8.7	<0.001*
BMI (Kg/m <sup>2</sup> )	22.0	2.4	24.0	2.7	25.3	2.8	<0.001*
HbA1c level	5.9	0.3	5.9	0.2	5.9	0.2	0.58

\*p&lt;0.05 statistically significant using Repeated Measure ANOVA

**Table III: Comparison of Weight, BMI and HbA1c Level at Baseline, 2<sup>nd</sup> Trimester and 3<sup>rd</sup> Trimester**

Parameters	Baseline to 2 <sup>nd</sup> Trimester		Baseline to 3 <sup>rd</sup> Trimester		2 <sup>nd</sup> Trimester to 3 <sup>rd</sup> Trimester	
	Mean Difference	SD	Mean Difference	SD	Mean Difference	SD
Weight (Kg)	-6.3*	0.6	-9.3*	1.7	-3.5*	1.1
BMI (Kg/m <sup>2</sup> )	-2.0*	0.9	-3.3*	1.2	-1.5*	1.4
HbA1c level	0.002	0.2	0.01	0.2	0.01	01

\*p&lt;0.05 statistically significant using Paired Sample t-test

**Table IV: Comparison of Metformin in 2<sup>nd</sup> and 3<sup>rd</sup> Trimesters With Weight Gain**

Weight Gain at 2 <sup>nd</sup> Trimester		Metformin at 2 <sup>nd</sup> Trimester				p-value
		500 mg OD		500 mg BID		
		Number	%	Number	%	
Weight gain at 2nd trimester was 6-Kg	Yes	3	60	49	51.6	0.71
	No	2	40	46	48.4	
Weight gain at 2nd trimester was 7-Kg	Yes	0	0	15	15.8	0.33
	No	5	100	80	84.2	
Weight gain at 2nd trimester was 8-Kg	Yes	1	20	5	5.3	0.17
	No	4	80	90	90.7	
Weight Gain at 3 <sup>rd</sup> Trimester		Metformin at 3 <sup>rd</sup> Trimester				p-value
		500 mg OD		500 mg BID		
		Number	%	Number	%	
Weight gain at 3rd Trimester was 10-Kg	Yes	3	60	24	25.3	0.09
	No	2	40	71	74.7	
Weight gain at 3rd trimester was 11-Kg	Yes	0	0	18	18.9	0.28
	No	5	100	77	81.1	

p-value was obtained by Mann Whitney U test

were 105.7±19.2 and 152.8±13.3 mg / dL respectively. Details are given in table I. In 76% of the patients GDM was diagnosed for the first time in pregnancy, and 77% had history of diabetes mellitus in first degree relatives. Eleven (11%) had previous history of intrauterine fetal death, 22% had miscarriages, 7% had NICU admissions, 10% had history of previous big size babies. Regarding dietary habits, on booking, 56% were consuming junk food once a week, 9% twice weekly and 5% on daily basis. Of the total, 97% - 98% of the patients were advised for lifestyle modifications and 30-minute walk 5-days a week. Table II shows the trend of weight, BMI and HbA1c level from baseline to the 3<sup>rd</sup> trimester. The weight and BMI were found significant. Mean change in parameters in different trimesters is given in table III. On comparison of weight gain at 2<sup>nd</sup> trimester with metformin 500 mg once a day, 60% women gained 6-kg weight in 2<sup>nd</sup> trimester. Details are given in table IV.

#### DISCUSSION:

This study was done on women with gestational diabetes mellitus which is defined as hyperglycemia detected in pregnancy either first time or after 20-weeks of gestation. The study aimed at achieving adequate glycemic control in all the trimesters of pregnancy with metformin along-with life style changes. The hyperglycemia in pregnancy is associated with adverse maternal outcome like pre-eclampsia, increase in BMI and abnormally high

HbA1c levels and may result in adverse fetal outcome.<sup>4</sup>

The International Diabetes Federation (IDF) reported in 2019 that 1 in every 6 pregnancies were effected by GDM and around 20 million neonates were affected worldwide.<sup>11</sup> GDM cases are usually managed conservatively by the life style modifications which include exercises, nutritional therapy and blood glucose monitoring.<sup>12</sup> A similar approach was used in our study with the addition of metformin. A study by Goh et al found that in addition to above life style changes, addition of metformin had better results and fewer maternal complication like pre-eclampsia, obesity and poor glycemic control as shown in our study.<sup>13</sup>

A study by Hyer et al compared the effect of metformin and insulin therapy. It was found that metformin group had less maternal weight gain (BMI) and better glycemic control which was statistically significant.<sup>14</sup> Our study also showed similar results. The use of metformin does not affect the weight of the pregnant women. It is reported as safe, cost effective, with better tolerability when taken orally and acceptability.<sup>15</sup> Metformin increases insulin sensitivity, reduces hepatic gluconeogenesis and peripheral utilization of glucose thus reducing blood glucose, with minimal risk of hypoglycemia.<sup>16</sup>

A meta-analysis of eleven randomized trials including 2,712 women with GDM found that metformin has a lower incidence of gestational hypertension which is an additional benefit.<sup>17</sup> In a study it was found that in all the patients with GDM treated with insulin alone, a higher maternal weight gain and therefore, the BMI were noted, as compared to groups treated with metformin combined with insulin.<sup>18</sup> Our study is considered a complimentary evidence on an important subject that affects not only the maternal wellbeing during pregnancy but also the fetal outcome. Prevalence of non-communicable diseases is on rise and WHO has raised a red flag. It is therefore important that awareness regarding diabetes mellitus in general and particularly in pregnancy be emphasized.

**Limitations of the study:** This is an observational study conducted at a tertiary care hospital with small sample size. However, it did support the findings of studies conducted earlier on same subject which is an important reproductive health issue.

#### CONCLUSION:

Metformin was found effective and well-tolerated glucose lowering agent that was safe in the management of GDM and improved the maternal outcome significantly in terms of weight gain and HbA1c levels.

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Ziaullah Khan: Data collection and literature review.  
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Naveeda Atif: Data analysis and literature review.
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