ORIGINAL ARTICLE

PREGNANCY CONSEQUENCES IN DIET CONTROLLED MILD GESTATIONAL HYPERGLYCEMIA

Rabia Arshad[1], Zahida Sheikh[2], Kausar Aamir[3], Nasim Karim[4], Tahira Asaad[5]

[1]Pharmacology Department, Altamash Institute of Dental Medicines, Karachi, [2]Department of Pathology, LUMHS, Jamshoro, Sindh, [3]Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute, JPMC, Karachi, [4]Pharmacology Department, Bahria University Medical and Dental College, [5]Pharmacology Department, Karachi Institute of Medical Sciences, Karachi.

ABSTRACT

Background: The evidence-based screening and management of gestational diabetes mellitus has continued to increase over the past several years. Therefore, our study is aimed to observe fetal and maternal outcomes in diet controlled mild gestational hyperglycemic patients and to compare them with normal controls.

Methods: After approval from IRB, 25 healthy females were enrolled as control (GROUP A) from antenatal clinic. While 31 mildly hyperglycemic females were enrolled from diabetic antenatal clinic, with RBS between 126-130 mg/dl or deranged fasting sugar level (GROUP B). They were educated for strict diet controlled nutritional therapy along with 30 minutes of walk thrice weekly. All patients were followed in antenatal clinics until term. Feto-maternal outcomes were tabulated for 25/31 females who completed the study, on SPSS 16.

Result: Patients were equally matching in height and weight in both groups. Fetal weight was significantly more in group B. Though non-significant but numerically more babies were delivered after 37 weeks in group B. At term there was higher FBS and HbA1C with significant number of surgical deliveries in group B than group A. HbA1C was significantly more in group B from enrollment towards term but was still less than 6%.

Conclusion: Mild hyperglycemic females on diet control therapy had significantly higher FBS and HbA1C levels at term, with increased fetal weight and percentage of cesarean deliveries in comparison to normal healthy controls.

Keywords: Mild Hyperglycemia; Gestational Diabetes; Nutritional Therapy; Fetal Outcomes; Maternal Outcomes; Pregnancy Consequences.

Corresponding Author:
Dr. Rabia Arshad
Pharmacology Department,
Altamash Institute of Dental Medicines,
Karachi, Pakistan.
Email: rabs78@gmail.com

INTRODUCTION

During pregnancy mother is exposed to multiple circulating maternal and placental hormones predisposing her to develop hyperglycemic state leading to diabetes in pregnancy, gestational diabetes mellitus (GDM). The women more likely to develop gestational glycemic disorders are those having obesity, unhealthy lifestyle and genetic predisposition for diabetes mellitus type 2 and history of GDM in previous pregnancies.[1] It is diagnosed in approximately 3-9% of pregnancies and the prevalence has risen in recent years due to sedentary life approach.[2] Altered glucose levels during gestation can lead to bad maternal outcomes.[3] Mothers with GDM have a higher risk of ending up with a caesarean section. Many a times they also develop gestational hypertension in the last trimester. It has been documented that they are more likely to develop Type II Diabetes Mellitus (DM) later in life.[4] There are increased rates of cardiovascular complications including obesity, high blood pressure and hyper-lipidemia in comparison to females with normal pregnancies[5].

Quality and quantity of food intake plays a meaningful role in the pre and postnatal outcomes during gestation. Diet control is foremost important man-

agement in glycemic syndromes. Patients diagnosed with hyperglycemia are kept on sugar control diet and are advised to follow a strict diet plan so as to maintain glucose levels near normal. The aim is to provide adequate calories to the mother and growing fetus without excessive weight gain and hyperglycemia. If a balance between nutrient needs and glucose control cannot be achieved, then pharmacological management is adopted which further can have side effect and financial load on the patient.[6] Nutrition control therapy is a self-management therapy. Education, support, and follow-up are required to assist the woman to make lifestyle changes essential to achieve successful controlled blood sugars in mild hyperglycemia[7].

Ricart et al. has documented that 9-19% of pregnant women have mild hyperglycemia during fasting only or upon administration of an oral glucose load which do not fulfill the criteria for pure GDM.[8] These patients are usually advised only nutritional controlled therapy and no pharmacological management. Consequently, if the therapy is not practiced properly, there can be bad feto-maternal outcomes compared to normal controls[9]. This case control study was conducted to observe the effect of maternal glucose intolerance, less severe than overt GDM, treated with diet control and exercise on fetal and maternal outcomes.

METHODS

This case control study was conducted in JPMC during Dec 2017-Dec 2018 as a part of Ph.D. (Pharmacology) and for this study, approval was provided by IRB (Institutional Review Board) JPMC, Karachi. Patients were enlisted after written informed consent from different hospitals in Karachi. 25 normal healthy pregnant females were enrolled as control (GROUP A). Confirmation for mild hyperglycemia was built with Oral Glucose Challenge Test and Oral Glucose Tolerance Test, according to WHO criteria[10]. This included women with no other co-morbid, aged between 18-40 year and diagnosed with mild gestational diabetes according to WHO criteria (fasting glucose more than 95 mg/dl, or at least two of three glucose values that exceeded the following: 1-hour of 180 mg/dl, 2-hour 155 mg/dl, 3-hour 140 mg/dl or patients with RBS from 126-130 mg/dl)10 since, 31 such females were assigned strict dietary treatment (GROUP B). They were advised to take 1800-2000 KCAL per day through provision of caloric charts prepared diet plans and 30 minutes of walk, thrice weekly.11 These patients were described in detail about use of calories and diet routine. They were re-evaluated after one week and if after diet therapy the blood sugar was in normal range (<126 mg/dl) they were advised to continue with it, otherwise excluded from the study and were given pharmacological management along with diet and exercise. Patients were followed fortnightly up until 32 weeks and then weekly till term. At enrolment [weight, HBA1C, FBS, RBS] and at term that is 36-37 weeks of pregnancy, maternal outcomes [weight, HBA1C, FBS, RBS, mode of delivery] and fetal outcomes [weight, Apgar score, delivery age] were evaluated. Finally, results were tabulated using SPSS 16 of 50 patients who completed the study with 25 patients in each group. Statistical tests were applied accordingly to evaluate the results.

RESULTS

Group A and group B were similar on patient's weight and age at the time of enrollment. There was a significant difference between fasting (FBS) and random blood sugar level (RBS) along with glycated hemoglobin (HbA1C) as one was control group and other was diabetic group (p= 0.00, 0.038, 0.00 respectively) (Table 1).

Table 1: Comparison of Maternal Characteristics Group A and B (N=50).

Variables	Group A n=25	Group B n=25	p-Value
	Mean±SD	Mean ±SD	
Age(Years)	29 ± 4.37	30.08±3.16	0.32
Weight(kg)	73.84±9.97	78.54± 6.93	0.059
FBS-1(mg/dl)	72.24±9.34	90.96±16.84	0.00*
RBS(mg/dl)	126.08±35.87	148.72±38.9	0.038*
HbA1C-1(%)	4.84±0.45	5.34 ±0.47	0.00*

*Group A: Control group = non- diabetic pregnancies; Group B: Diet control and exercise GDM group = diabetic pregnancies; * statistically significant (Independent t- test applied); FBS1: fasting blood sugar level at enrollment; HbA1C-1: glycated hemoglobin at enrollment.*

Mean weight of the baby at birth was significantly more in group B when compared to group A (p=0.034). Apgar score was non-significant between the groups (p=0.46). Though the delivery age between group A and B was non-significant but numerically more babies were delivered after 37 weeks in group B (16% vs. 32%, p=0.18). Fasting blood sugar level and HbAIC was significantly more in group B when compared to Group A (p=0.00 and 0.00 respectively). There was significantly more number of surgical deliveries in Group B as compared to Group A (40% vs. 28%, p=0.034) (Table 2).

Table 2: Maternal Outcomes at 36-37 Weeks of Pregnancy Comparison between Group A and B (n=50).

Fetal outcomes	Group A n=25	Group B n=25	p-Value
	Mean±SD	Mean±SD	
Weight of the baby(kg)	2.9±4.3	3.09±0.3	0.034*
Apgar score	8.84±0.62	8.56±0.8	0.46
	n (%)	n (%)	
Delivery age			
37 weeks	21(84%)	17(68%)	0.18
after 38 weeks	4(16%)	8(32%)	
Maternal outcomes	Mean±SD	Mean±SD	
HBAIC-2 (%)(36weeks)	4.97±0.45	5.74±0.49	0.00*
FBS -2 (36 weeks)	76.48±9.65	88.88±8.7	0.00*
	n (%)	n (%)	
Mode of delivery			
Normal vaginal	18(72%)	11(44%)	0.045*
Assisted delivery	0	4(16%)	
Cesarean section	7(28%)	10(40%)	
• Cesarean due to feto maternal disproportion	0	4(16%)	

*Group A: Control group = non- diabetic pregnancies; Group B: Diet control and exercise group GDM = diabetic pregnancies; * statistically significant (chi square and Independent t- test); NA: Chi square test not applicable.*

When comparison was done for the FBS and HbA1C in Group A at enrollment and at term the results were non-significant (p= 0.056, 0.73 respectively). There was non-significant differences for group B, for FBS (p=0.48) whereas HbA1C was statistically significant (p=0.00) when compared at enrollment and at 37 weeks of gestation (Table 3).

Table 3: HbA1C and FBS AT Enrollment and at 36-37 Weeks of Pregnancy Group A vs. B N=50.

Groups	At Enrollment	At Term	p-Value
	Mean±SD	Mean ±SD	
Group A FBS	72.24± 9.34	76.12±9.98	0.056
Group A HbA_1C	4.84±0.45	4.95±0.43	0.73
Group B FBS	90.96±16.84	88.88±8.79	0.48
Group B HbA_1C	5.34±0.47	5.73±0.48	0.00*

*Group A: Control group = Non-diabetic pregnancies, Group B: Diet control and exercise group GDM = diabetic pregnancies, HbA1C: Glycated hemoglobin; FBS: fasting blood sugar, *statistically significant result (Paired t- test applied).*

DISCUSSION

Mild hyperglycemia is the commonest metabolic problem occurring during pregnancy due to circulating maternal hormones, which increases insulin resistance. The diagnostic criteria utilized is derived from WHO which states that fasting glucose more than 95 mg/dl, or at least two of three glucose values after 75-g OGTT exceeding the following: 1-hour of 180 mg/dl, 2-hour 155 mg/dl, 3-hour 140 mg/dl, confirms patient as gestational diabetic. This is still utilized in many of the countries including ours. The Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study,[11] a large-scale multinational epidemiologic study, demonstrated that risk of adverse maternal, fetal, and neonatal outcomes continuously are at rise as a function of maternal glycemia at 24-28 weeks, even within ranges previously considered by WHO normal for pregnancy. These results have led to careful reconsideration of the diagnostic criteria for GDM. An international consensus group with representatives from multiple obstetrical and diabetes organizations, including ADA, developed revised recommendations for diagnosing GDM. The group recommended that all women not known to have diabetes undergo a 75-g OGTT at 24–28 weeks of gestation fasting glucose more than 92 mg/dl, or glucose values that exceeding after 1-hour of 180 mg/dl or after 2-hour 153 mg/dl12 which is slightly different to WHO criteria.

For mild hyperglycemic patients during pregnancy, the group considered in this particular study, diet control is the foremost important management. However, it has been seen that only diet control in many patients is not sufficient to decrease glucose level.[13] Our both normal control and mildly hyperglycemic groups were similar in the age and weight, whereas these patients had different FBS, RBS and HbA1C level before the start of treatment. Same groups were taken by Weijers in his study.[14]

Mean weight of the baby at birth was significantly more in mild hyperglycemic group controlled with diet therapy. Durnwald also documented that females with mild hyperglycemia, kept on diet control had babies with more birth weight and large for their gestation age.[15] Same were the results from Adams, that females with mild GDM and on controlled diet only give birth to babies with more weight as compared to non-diabetic females (15% vs. 8%).[16] Both of these studies are similar to our study results as weight of the newborns was significantly more in GDM with diet controlled group (p= 0.034*).

Moreno also described in her study that there is no improvement in pregnancy outcomes with strict diet control therapy in GDM.[17] In contrast to this, another study by Moses documented that women assigned to a low glycemic index diet during pregnancy gave birth to infants who were lighter (3408 ± 78 g vs. 3644 ± 90 g) and had a lower incidence of large for gestational age, compared to women given a high glycemic index diet, suggesting that the concept of less calories is valid in GDM pregnancy. He suggested that reduction not only in simple carbohydrates but also in fat intake is advisable. He further emphasized to have dietary intake over six meals daily, with three main meals and three snacks, in order to avoid large carbohydrate loads at any time.[18]

In our study Apgar score was non-significant between the groups (p=0.46). Homko also stated the same fact that in his study Apgar score did not show any significant difference between both the groups.[19] The study results indicated that the delivery age between normal control and mild hyperglycemic was non-significant when two groups were compared but numerically more babies were delivered after 37 weeks in diabetic group (16% vs.32%, p=0.18). A study by Durnwald confirmed that the babies in only diet control group delivered after 37 weeks of pregnancy as in his study results mean gestational age was 39.1 weeks in diet controlled GDM group15, whereas Black stated that women with elevated post glucose load values and mild hyperglycemia were at higher risk for preterm deliveries.[20]

Fasting blood sugar level and HbAIC at 36 weeks of pregnancy were significantly more in diet controlled GDM group when compared to normal controls, indicating that adequate diet control and exercise was not sufficient to control the blood sugar levels in mild hyperglycemics (p=0.00 and 0.00 respectively). It is therefore required to educate patients well for strict diet control and regular glucose monitoring. Balaji stated that if glucose intolerance is detected in early pregnancy, HbA1c level would be helpful to differentiate between a pre-GDM and GDM. If the HbA1C level is more than 6%, there can be adverse pregnancy outcomes. HbA1C level may serve as a prognostic value. If HbA1C level is used to monitor glucose control in pregnancy, the target level to be maintained is 5.3% and in our study results the mean HbA1C was 5.74 % in diet control group which is less than 6%.[21]

As discussed in our study results there were significantly a greater number of surgical deliveries in diet controlled GDM group when compared controlled (40% vs. 28%, p=0.034). Kaymuk also described in his research that mild hyperglycemia leads to more cesarean sections as compared to normal controls and he finally concluded that these females are at increased risk for surgical deliveries.[22] Scholl stated that approximately 14.4% females with blood sugar levels between 90-130 mg/dl had cesarean deliveries which is less than our documented results.[23] Kampan studied in Malaysian females and have stated that 23.7 % of diet controlled GDM had surgical deliveries.[24]

When comparison was done for the FBS and HbA1C in normal control at enrollment and at term the results were non-significant. There were non-significant differences for diet controlled GDM, for FBS (p=0.48) whereas HbA1C was statistically significantly more (p=0.00) at 37 weeks of gestation but still less than 6%. Louie documented in his research on nutritional controlled group with low glycemic diet that at enrollment the HbA1C was mean 5.4% which rose only to 5.5 % at term.[25] Pirc described in his study that mild gestational diabetes is a common complication in pregnancy, affecting up to 9% of pregnant women and can lead to significant maternal, fetal and neonatal morbidities that results from disturbances of glucose homeostasis in pregnancy. He also concluded that treatment of mild GDM with good diet control and exercise could surely reduce adverse perinatal outcomes.[26]

Good glycemic control can be achieved in mild hyperglycemia with nutritional therapy and mild exercise with no drug intervention in pregnancy. This requires adequate patients counseling and education. Recent researches have shown that many smart phone apps are extremely helpful in maintaining good glycemic control along with standard care and can be an open avenue for new researchers[27,28].

CONCLUSION

Mild hyperglycemic females on diet control therapy had significantly higher FBS and HbA1C levels at term, with increased fetal weight and percentage of cesarean deliveries in comparison to normal healthy controls.

ACKNOWLEDGEMENTS

I want to convey thanks to Dr. Haleema, Head of Gynae and Obstetric Department, JPMC for clinical help and supervision. Many thanks to Mr. Owais from DIMC, DUHS for statistical help, Mr. Adeel and Mr. Adnan from BMSI, JPMC for immunological and histo-pathological expertise.

CONFLICT OF INTEREST

There is no conflict of interest between the authors.

AUTHORS CONTRIBUTION

Rabia Arshad conceived, designed, conducted research and did main write up of manuscript. Dr. Zahida Sheikh helped in data collection and statistical analysis. Kausar Aamir is the supervisor of the study. Nasim Karim helped in designing the methodology of the study and provided editing and final approval of manuscript. Tahira Assad helped in data collection, write up and proof reading of manuscript.

REFERENCES

1. Serlin DC, Lash RW. Diagnosis and management of gestational diabetes. Am Fam Physician. 2009; 80(1):57-62.
2. Catalano PM, Kirvan JP, Mouzon SH, King J. Gestational diabetes and insulin resistance: Role in long- and short-term complications for mother and fetus. J Nutr. 2003 ;133 :1638-78.
3. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008; 358:1991-2002.
4. Ben-Haroush A, Yogev Y and Hod M. Epidemiology of gestational diabetes mellitus and its association with Type 2 diabetes. Diabet Med. 2003; 21:103-13.
5. Langer O, Yoger Y, Most O, Venakes EM. Gestational diabetes: the consequences of not treating. Am J Obstet Gynecol. 2005; 192(4): 989-97.
6. Reader DM. Medical Nutrition Therapy and Lifestyle Interventions. Diabetes Care. 2007; 30 (2): S188–S93.
7. Reader D, Splett P, Gunderson E. Impact of gestational diabetes mellitus nutrition practice guidelines implemented by registered dietitians on pregnancy outcomes. J Am Diet Assoc. 2006; 106:1426–33.
8. Ricart W, Lopez J, Mozas J, Pericot A, Sancho MA, Gonzalez N et al. criteria for diagnosis of gestational diabetes mellitus in Spain. Diabetologia. 2005; 48:1135– 44.
9. Kayal A, Mohan V, Malanda B, Anjana RM, Bhavadharini B, Mahalakshmi MM, et al. Women in India with Gestational Diabetes Mellitus Strategy (WINGS): Methodology and development of model of care for gestational diabetes mellitus (WINGS 4). Indian J Endocrinol Metab. 2016;20(5):707–715.
10. Arshad R, Khanam S, Shaikh F, Karim N. Feto-maternal outcomes and Glycemic control in Metformin versus insulin treated Gestational Diabetics. Pak J Med Sci. 2017;33(5):1182–1187.
11. Metzger BE, Lowe LP, Dyer AR et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358:1991–2002.
12. Diagnosis and Classification of Diabetes Mellitus. American Diabetes Association. Diabetes Care. 2013; 36 (1): S67-S74.
13. Chen X, Scholl TO, Leskiw M, Savallie J, Stein TP. Differences in Maternal Circulating Fatty Acid Composition and Dietary Fat Intake in Women with Gestational Diabetes Mellitus or Mild Gestational Hyperglycemia. Diabetes Care. 2010; 33(9): 2049 54.
14. Weijers RNM, Bekedam DJ, Smulders YM. Determinants of Mild Gestational Hyperglycemia and Gestational Diabetes Mellitus in a Large Dutch Multi-ethnic Cohort. Diabetes Care 2002; 25:72–7.
15. Durnwald CP, Mele L, Spong CY, Ramin SM, Varner MW, Rouse DJ, et al. Glycemic Characteristics and Neonatal Outcomes of Women Treated for Mild Gestational Diabetes. Obstet Gynecol. 2011; 117(4): 819–27.
16. Adam KM, Li H, Nelson RL, Ogburn PL Jr., Danilenko-Dixon DR. Squeal of un-recognized gestational diabetes. AJOG. 1998; 178(6): 1321–32.
17. Moreno-Castilla C, Hernandez M, Bergua M, Alvarez M C, Arce M A, Rodriguez K, et al. Low-Carbohydrate Diet for the Treatment of Gestational Diabetes Mellitus. A randomized controlled trial. Diabetes Care. 2013; 36(8): 2233-38.
18. Moses RG, Calvert D. Pregnancy Outcomes in Women without Gestational Diabetes Mellitus Related to the Maternal Glucose Level: Is there a continuum of risk? Diabetes Care. 1995; 18(12): 1527-33.
19. Homko JC, Sivan E, Reece EA. The impact of self-monitoring of blood glucose on self-efficacy and pregnancy outcomes in women with diet controlled gestational diabetes. Diabetes Educ. 2002; 28(3):435-43.
20. Black MH, David A, Xiang AH, Anny H, Lawrence JM. Sacks Clinical Outcomes of Pregnancies Complicated by Mild Gestational Diabetes Mellitus Differ by Combinations of Abnormal Oral Glucose Tolerance Test Values. Diabetes Care. 2010; 33(12): 2524-30.
21. Balaji V, Seshiah V. Management of Diabetes in Pregnancy. J Assoc Physicians India. 2011; 59: 33-9.
22. Kaymuk O, Iskender CT, Ustunyurk E, Yildiz Y, Doganacy M, Danisman N. Retrospective evaluation of perinatal outcomes in women with mild gestational hyperglycemia. J Obstet Gynecol Res.

2011;37(8):986-91.
23. Scholl TO, Sowers M, Chen X, Lenders C. Maternal glucose concentration influences fetal growth, gestation and pregnancy complications. Am J Epidemiol. 2001; 154(6): 514-20.
24. Kampan N, Azman H, Hafiz I, Mohammad H, Yee CS, Ghani NAA et al. Outcome Of pregnancy among Malaysian women with Diabetes Mellitus - A single center experience. Malaysian J Public Health Med. 2013,13 (2):1-10
25. Louie JCY, Markovic TP, Perera N, Foote D, Petocz P, Ross GP et al. Investigating the effects of a Low–Glycemic Index diet on pregnancy outcomes in Gestational Diabetes Mellitus. Diabetes Care. 2011; 34:2341–46.
26. Pirc LK, Owens JA, Crowther AC, Willson K, De Blasio MJ, Robinson JS. Mild gestational diabetes in pregnancy and the adipoinsular axis in babies born to mothers in the ACHOIS randomized controlled trial. BMC Pediatr. 2007; 7:18.
27. Borgen I, Garnweidner-Holme LM, Jacobsen AF, Bjerkan K, Fayyad S, Joranger P et al. Smartphone application for women with gestational diabetes mellitus: a study protocol for a multicenter randomized controlled trial. BMJ. 2017; 7: 013117.
28. Mackillop LH, Bartlett K, Birks J, Farmer AJ, Gibson OJ, Kevat DA et al. Trial protocol to compare the efficacy of a smartphone-based blood glucose management system with standard clinic care in the gestational diabetic population. BMJ. 2016; 6: 009702.