



DIABETES MELLITUS DURING PREGNANCY IS A RISK FACTOR FOR HYPERTENSION.

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ABSTRACT:

Introduction: According to reports, one in every ten pregnancies in the world is accompanied with diabetes, with GDM accounting for 90% of the cases. GDM rates in India are anticipated to be 10-15%, with a growth to 20% expected. There is a significant positive relationship between maternal hyperglycemia and unfavourable maternal outcome, with hypertension in pregnancy having the highest link. The current investigation aims to uncover the link between GDM and hypertension during pregnancy.

Methods: A prospective observational study of 1000 pregnant women was conducted. Among these, 230 fulfilled the updated IADPSG criteria for GDM, whereas the others were classified as normoglycemic. The pregnancy associated hypertension (PAH) category includes women with preeclampsia and gestational hypertension. The risk of PAH was assessed in women with normoglycemia and GDM, and maternal demographic variables related with it were discovered.

Result: There were 58 (3.5%) women with PAH. When compared to women with GDM, normoglycemic women had a lower rate of PAH (5.1% vs 7.2%, $p > 0.05$). The probability of pre-eclampsia in GDM patients was considerably higher than in normoglycemic women ($p < 0.05$). Women with GDM and PAH also had the highest incidence of pregnancy after 35 years, obesity, primiparity, and caesarean sections.

Conclusion: This study found that GDM is linked to an increased risk of PAH. The common pathophysiology proposed for both GDM and hypertension in pregnancy is a pre-pregnancy susceptibility to beta cell malfunction, which may be masked by the growing insulin resistance during pregnancy. Early detection and careful monitoring of women with GDM for the development of PAH are critical.

Key words: GDM and PAH

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is a term that refers to abnormal glucose tolerance that occurs or is first recognized during pregnancy. GDM has long been linked to obstetric and neonatal complications, most notably higher

infant birth weight, and is now being recognized as a risk factor for future maternal and offspring cardio metabolic disease. GDM prevalence continues to rise globally as a result of epidemiological factors such as rising obesity rates in women of reproductive age, rising

maternal age, and the implementation of revised International Association of Diabetes and Pregnancy Study Groups criteria and diagnostic procedures for GDM. Given that GDM is now one of the most common complications of pregnancy, the current lack of international consensus on its diagnosis reflects its complex historical evolution and pragmatic antenatal resource considerations. Regardless, the modern clinical approach to GDM should be guided not only by its immediate complications, but also by its long-term prognosis.

According to reports, one in every ten pregnancies in the world is associated with diabetes, with GDM accounting for 90% of these cases. In India, one of the world's most populous countries, the incidence of GDM is estimated to be 10-15%, which is higher than in the West. The incidence of GDM is expected to rise to 20%, implying that one in every five pregnant women will be affected. Insulin resistance is a physiological process in a normal pregnancy, and the hyperinsulinemia that results in predisposed women can manifest as gestational diabetes mellitus and pregnancy hypertension. As a result, insulin resistance plays an important role in the development of hypertensive disorders of pregnancy, as well as an increased risk of future hypertension and cardiovascular disease in these women.

Gestational diabetes mellitus and hypertension in pregnancy have both been proposed as early manifestations of metabolic syndrome, which includes hypertension, diabetes, and obesity. Offspring of women with GDM are also at a higher risk of developing type 2 diabetes mellitus later in life. The current study is an attempt to uncover the link between GDM and hypertension in pregnancy, blaming the two on a common etiologic pathway such as insulin resistance and risk factors such as age, obesity,

and parity. However, these common etiologic triggers for the emergence of these disorders have not been adequately tested.

Material and Methodology:

This prospective observational study was conducted at a tertiary care centre in the department of obstetrics and gynaecology on all antenatal patients except those who had pre-existing diabetes or overt diabetes. A single-step approach based on IADPSG recommendations was used to diagnose gestational diabetes mellitus. A standard oral glucose tolerance test (OGTT) was performed between 24 and 28 weeks of gestation, according to the study. OGTT was performed at the first antenatal visit in pregnant women with high risk factors for GDM, such as age >35years, BMI>30kg/m², a family history of diabetes mellitus (in first degree relatives), previous H/O intrauterine foetal demise, and/or previous H/O macrosomic baby, and then again at 24-28wks if found to be normal.

Standard OGTTs were done after an overnight fast (8-14 hours) to determine whether pregnant women had gestational diabetes. After 1 hour and after 2 hours, 75 g of anhydrous glucose was given in 250-300 ml water and plasma glucose was measured. All pregnant women who met revised International Association of Diabetes and Pregnancy Study Groups criteria for gestational diabetes were categorized as having GDM, while those who had normal OGTTs were categorized as normoglycemics (Table 1). All patients who were diagnosed with GDM were treated with medical nutritional therapy, oral hypoglycemics, or insulin, depending on their needs, and were followed up according to institutionally established GDM treatment standards.

Table 1: IADPSG Consensus Panel guideline for diagnosing GDM

	Plasma Glucose Threshold (mg/dl)
Fasting	92
1-hour	180
2-hours	153

Information from the usual obstetric examinations and routine urine analyses was used to detect gestational hypertension and preeclampsia. In women with proteinuria on the dipstick test, 24-hour urine protein levels were measured. According to the American College of Obstetricians and Gynecologists definition, preeclampsia-eclampsia was defined as the presence of proteinuria after 20 weeks of gestation in association with hypertension. The Working Group on High Blood Pressure in Pregnancy defines gestational hypertension as a systolic blood pressure of 140 mmHg or greater after 20 weeks of gestation. Diagnosis of gestational hypertension (BP values >140 or >90 mm Hg for systolic or diastolic BP, respectively, after the 20th week of gestation without clinical record of hypertension previous to 20th week of gestation and prior to pregnancy) or preeclampsia (gestational hypertension with any one or more of these - proteinuria >300 mg in 24 hours of urine collection/thrombocytopenia with platelets $<100,000$ per mm^3 /impaired liver functions in form of elevated transaminases twice the normal levels/new development of renal insufficiency in absence of other diseases or pulmonary oedema/new onset of cerebral or visual disturbances, diagnosed after the 20th week of gestation in a previously normotensive women) was done with information from the routine obstetric examinations. Women with preeclampsia or gestational hypertension were included in the PAH group. These patients were managed and followed up according to standard guidelines for the condition.

The specific objectives of our study were:

1. The purpose of this research was to document the occurrence of GDM and compare the risk of pre-eclampsia and PAH in women with normal glucose levels.
2. Demographic factors related to the prevalence of GDM and PAH are to be identified.
3. To examine if there are any differences in maternal and fetal characteristics between the normoglycemia and GDM groups in relation to PAH.

Statistical Analysis: SPSS version 19 was used for statistical analyses, and chi-square values were used to examine the correlations among

variables. p-values were calculated with a significance level of $p = 0.05$ and a 95% confidence interval.

Results

All the women who had an OGTT and were pregnant were included in the study. Of the 1000 participants, 270 had GDM and 730 had normal results. However, the mean age of those with GDM was 24.80 years (SD-3.938), which was higher than the usual value (23.63 years; SD-3.531). More than twice the number of women over 35 years in the GD group had GDM ($p < 0.05$) (Table 2).

Of the participants, 58 (3.5%) women had pregnancy-associated hypertension (PAH), which included gestational hypertension and pre-eclampsia. In the normoglycemic women, 45 (5.1%) had PAH as compared to 09 (7.2%) women with GDM. Of the 45 women with PAH in the normoglycemic group, 25 had gestational hypertension and 19 had pre-eclampsia. There were 11 women with pre-eclampsia in the GDM group and 2 with gestational hypertension. In the control group, 6 women were chronic hypertensive and they were not compared for outcomes. Though there was no statistical significance between GDM and PAH ($p = 0.25$), the association between GDM and pre-eclampsia was significantly more than between normoglycemia and pre-eclampsia ($p < 0.05$). Conversely, there was no statistical significance between PAH and pre-eclampsia ($p = 0.28$).

Women with gestational diabetes mellitus (GDM) and PAH had the highest rates of pregnancy after 35 years, obesity, and primiparity in a comparison of women with or without hypertension. These risk factors apparently increase the risk of PAH in GDM patients. The infants of normoglycemic women and those with PAH had the lowest mean birth weight. Birth weight of babies of women with GDM and PAH was observed to be normal (Table 3). Well-controlled GDM not only prevents adverse fetal outcome in the form of abnormal birth weight and intrauterine fetal demise, but also prevents adverse fetal outcome in terms of obesity and type 2 diabetes in future life stage.

Table 2: Characteristics of women with or without gestational diabetes mellitus

Sr No.	Characteristics	Normoglycemic (n=730 women)	GDM (n=230 women)	p-value
1.	Associated PAH, Gest HT & PE (%)	45(5.1%)	09 (7.2%)	.25
2.	Mean Age(yrs)	23.63(SD-3.53)	24.80(SD-3.93)	.001
3.	Age >35(%)	13 (1.2%)	1 (0.9%)	.015
4.	BMI (%)	5(0.5%)	1(1.5%)	.21
5.	Nulliparas (%)	512(55.5%)	62(50.5%)	.24

Table 3: Comparison of characteristics in women with normoglycemia & GDM with respect to presence or absence of PAH

	Normoglycemic	ormoglycemic with PAH	p-value
Age >35yrs (%)	10(1.2%)	1(3%)	.11
BMI>30(%)	3(0.2%)	2(3.5%)	.00
Nulliparas (%)	421(54.3%)	30 (65%)	.03
Caesarean deliveries (%)	212(21.9%)	19(39%)	.001
Mean Birth Weight, kg(SD)	2.67(0.39)	2.36(0.44)	.000
	GDM	GDM with PAH	p-value
Age >35yrs (%)	1(0.6%)	1(9%)	.019
BMI>30(%)	1(0.6%)	1(9%)	.019
Nulliparas(%)	55(47.6%)	6(60%)	.19
Caesarean deliveries (%)	38(32.4%)	5(50%)	.16
Mean Birth Weight, kg(SD)	2.59(0.59)	2.84(0.42)	.13

Discussion:

Women who are diagnosed with GDM during pregnancy have an increased risk of developing pregnancy-induced hypertension. Ingestion of refined carbohydrates during the gestational period has been shown to increase the risk of developing gestational hypertension, mild preeclampsia, and severe preeclampsia, according to Bryson et al. A study found that women with gestational diabetes were 1.5 times more likely to develop these disorders than other women.

In the present study this risk was 5.1% in normoglycemic women increasing to 7.2% on association with GDM, although the difference was not significant. This may be due to a smaller sample size of our study. In contrast, the research discovered that women with GDM have a much higher chance of developing preeclampsia than the normoglycemics. A significantly increased risk of preeclampsia was reported in a cohort study among mothers with

gestational diabetes compared to those without it. The authors evaluated the association between gestational diabetes mellitus and hypertensive diseases after matching for age, body mass index, parity, and pregnancy duration and found that hypertension was more prevalent in gestational diabetes mellitus patients.

With several studies pointing to a link between GDM and hypertension during pregnancy, there is a chance that the two disorders share pathology. GDM has pre-pregnancy origins in beta cell dysfunction, which may be obscured by pregnancy's progressive insulin resistance. Endothelial damage and inflammation may be caused by insulin resistance, which leads to hyperglycemia. Indeed, it has been proposed that insulin resistance during pregnancy is a common trigger that leads to GDM and/or PAH in predisposed women. There have also been reports of several common pregnancy maladaptations that may be to blame for the link between the two disorders. Endothelial

dysfunction (lower flow-mediated dilation), increased oxidative stress (low total antioxidant status, high free radicals), and dyslipidemia (high triglycerides) are all possible consequences of hyperglycemia-induced inflammation and endothelial damage. However, none of these pathophysiologies have been proven.

Another finding from our study indicates that risk factors for GDM, such as age >35 years, obesity, and nulliparity, are more prevalent in women with PAH, indicating that all of these factors are related with an increased risk of PAH. According to the findings of a relatively large prospective Brazilian study, gestational diabetes and hypertension in pregnancy increase with increasing age and adiposity and decrease with decreasing parity, demonstrating that these risk factors are common to both disorders and supporting the idea that the causes of the two disorders are similar.

Gestational diabetes and hypertension in pregnancy are thought to be precursors to the development of metabolic syndrome, which comprises hypertension, diabetes, and obesity. This could be attributed to the increased prevalence of risk variables in pregnancy with GDM and/or PAH, which are frequent with metabolic syndrome risk factors such as advanced age, obesity, and excessive weight gain. As a result, the increased risk of hypertension during pregnancy in women with gestational diabetes may point to an underlying shared pathophysiology linked to the development of metabolic syndrome later in life. There is also a link between pregnancy-related hypertension and an increased risk of developing hypertension, ischemic heart disease, thromboembolic events, and diabetes later in life. If an intervention for optimal GDM control during pregnancy can minimise the chance of PAH, it can reduce the long-term negative effects associated with these two illnesses.

Conclusion:

This research reveals that hypertension during pregnancy is more common in women with gestational diabetes. Early detection and better monitoring and follow-up of women with GDM

for the development of this condition are required. Further research into the underlying common pathophysiology of these two pregnancy illnesses, increasing insulin resistance, may assist doctors improve early identification, prevention, and treatment of GDM and hypertension in pregnancy, as well as their long-term detrimental effects.

References:

1. Rani PR, Begum J. Screening and Diagnosis of Gestational Diabetes Mellitus, Where Do We Stand. *J Clin Diagn Res.* 2016;10(4):QE01-QE4. doi:10.7860/JCDR/2016/17588.7689
2. Buchanan TA, Xiang AH, Page KA. Gestational diabetes mellitus: risks and management during and after pregnancy. *Nat Rev Endocrinol.* 2012;8(11):639-649. doi:10.1038/nrendo.2012.96
3. Sweeting, A., Wong, J., Murphy, H. R., & Ross, G. P. (2022). A Clinical Update on Gestational Diabetes Mellitus. *Endocrine reviews*, 43(5), 763–793. <https://doi.org/10.1210/endrev/bnac003>
4. Swaminathan G, Swaminathan A, Corsi DJ. Prevalence of Gestational Diabetes in India by Individual Socioeconomic, Demographic, and Clinical Factors. *JAMA Netw Open.* 2020;3(11):e2025074. Published 2020 Nov 2. doi:10.1001/jamanetworkopen.2020.25074
5. Plows JF, Stanley JL, Baker PN, Reynolds CM, Vickers MH. The Pathophysiology of Gestational Diabetes Mellitus. *Int J Mol Sci.* 2018;19(11):3342. Published 2018 Oct 26. doi:10.3390/ijms19113342
6. Sullivan SD, Umans JG, Ratner R. Hypertension complicating diabetic pregnancies: pathophysiology, management, and controversies. *J Clin Hypertens (Greenwich).* 2011;13(4):275-284. doi:10.1111/j.1751-7176.2011.00440.x
7. Choudhury, A. A., & Devi Rajeswari, V. (2021). Gestational diabetes mellitus - A metabolic and reproductive disorder. *Biomedicine & Pharmacotherapy*, 143, 112183. <https://doi.org/10.1016/j.biopha.2021.112183>

8. Lee KH, Han YJ, Chung JH, et al. Treatment of gestational diabetes diagnosed by the IADPSG criteria decreases excessive fetal growth. *Obstet Gynecol Sci.* 2020;63(1):19-26. doi:10.5468/ogs.2020.63.1.19
9. Bryson CL1, Ioannou GN, Rulyak SJ, Critchlow C. Association between gestational diabetes and pregnancy-induced hypertension. *Am J Epidemiol.* 2003 Dec 15;158(12):1148-53.
10. Nerenberg, K. A., Johnson, J. A., Leung, B., Savu, A., Ryan, E. A., Chik, C. L., & Kaul, P. (2013). Risks of gestational diabetes and preeclampsia over the last decade in a cohort of Alberta women. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*, 35(11), 986–994. [https://doi.org/10.1016/S1701-2163\(15\)30786-6](https://doi.org/10.1016/S1701-2163(15)30786-6)
11. Hossein-nezhad A., Mirzaei K., Ahmadi S, Maghbooli Z, Karimi F Comparison of incidence of pregnancy Induced hypertension in gestational diabetes mellitus and healthy pregnant women. *Iranian Journal of Diabetes and Lipid Disorders*; 2011; Vol 10, pp 1- 9.
12. Wendland EM, Duncan BB, Belizán JM, Vigo A, Schmidt MI. Gestational diabetes and pre- eclampsia: common antecedents? *Arq Bras Endocrinol Metabol.* 2008;52(6):975-984.
13. Vohr, B. R., & Boney, C. M. (2008). Gestational diabetes: the forerunner for the development of maternal and childhood obesity and metabolic syndrome?. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians*, 21(3), 149–157. <https://doi.org/10.1080/14767050801929430>