An Analysis of Maternal Factors in Normal Pregnancy and Pregnancy with Gestational Diabetes Mellitus

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ABSTRACT

BACKGROUND

Gestational Diabetes Mellitus (GDM) is a global public health concern with potential implications for the health of a mother and her offspring. Several maternal factors are strongly related to GDM. This study aims at analysing maternal factors associated to GDM.

METHODS

This comparative study was conducted in the Department of Obstetrics and Gynaecology, Institute of Maternal and Child Health, Medical College, Calicut. A total of 200 subjects were included in the study. The subjects were divided into two groups comprising 150 normal pregnant women and 50 pregnant women who were diagnosed to have GDM. Age, gravida, parity, detailed obstetric history, and history of any treatment were recorded. Height and weight were recorded. BMI was calculated using the formula, Weight in Kg/Height in m^2. Blood pressure too was recorded. All statistical data were analysed using SPSS software version 16. Continuous variables were expressed as mean ± standard deviation. Qualitative data was expressed as percentage. Independent t test was used for comparing quantitative data between the two groups. Analysis was done to compare relation of age, BMI, gravida and blood pressure in GDM and normal pregnancy.

RESULTS

The mean age in women with GDM was found to be 26.24 years and that in controls was 23.77 years; the difference was statistically significant. The mean value of Body Mass Index of women with GDM was 26.98 Kg/m^2 and that in normal pregnant women was 23.42 Kg/m^2; the difference was highly significant. No significant relation was observed between gravida and occurrence of GDM. The mean systolic blood pressure in women with GDM was 122.04 mm of Hg and that in pregnant controls was 113.17 mm of Hg (p value < 0.01, significant). The mean diastolic blood pressure in women with GDM was 79.76 mm of Hg and that in pregnant controls was 73.13 mm of Hg with a significant p value of <0.01.

CONCLUSIONS

GDM women were found to be overweight in comparison with the control group. Status of gravid was found to have no significant relation with GDM. The blood pressure was significantly higher in GDM even though it was within the normal range.

KEYWORDS

Glucose tolerance, Gestational Diabetes, Blood Glucose, Pregnancy**,** Body Mass Index, Blood Pressure

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BACKGROUND

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. Women with clinical characteristics consistent with a high risk of GDM should be properly identified.

Fourth International Workshop Conference on GDM has recommended a screening strategy based on risk assessment.[1] Shahrood et al, Hill et al has researched on relationship of maternal age and occurrence of GDM.[2,3,4] The occurrence of diabetes in Indians was found to be 10 to 15 years earlier than in western population in a study comparing the two.[5] The UK Prospective Diabetes Study concluded that Asians develop type 2 diabetes earlier than Afro-Caribbean and White Caucasians.[6]

Body Mass Index is a factor highly implicated in the pathogenesis of gestational diabetes. The prevalence of obesity in Southeastern Asian women was 0.9%.[7] It has been suggested that specific BMI classifications should be validated for Asian women.[8] Likewise this research tried to analyse many other maternal factors like gravid, BP etc associated with GDM.

We wanted to study the relation of age, body mass index, gravida and blood pressure in normal pregnancy and gestational diabetes mellitus.

METHODS

The study was conducted in the Department of Obstetrics and Gynaecology, Institute of Maternal and Child Health, Medical College, Calicut.

A total of 200 subjects were included in the study. The subjects were divided into two groups comprising of 150 healthy pregnant women with no history of GDM and 50 pregnant women with GDM. The GDM was diagnosed by oral glucose challenge test (OGCT). For OGCT, they were given 50 gm of glucose in about 200 mL of water over 2 to 3 minutes. Exactly at 1 hour, 1 ml of blood is drawn from a forearm vein using a disposable syringe under aseptic precautions into a clean dry bottle containing oxalate. The blood glucose is determined by the Glucose Oxidase/Peroxidase method. (GOD/POD method). Women with diabetes, hypertension and renal disease diagnosed before pregnancy were excluded from the study.

A detailed history was taken. Age, gravida, parity, detailed obstetric history and history of any treatment were recorded. Height and weight were recorded. BMI was calculated using the formula, Weight in Kg/Height in m^2. Blood pressure too was recorded.

Study was approved by Human Ethical Committee and Review Board of Institution. Study subjects were counselled separately about the study and a written consent was procured from them.

All statistical data were analysed using SPSS software version 16. Continuous variables were expressed as mean ± standard deviation. Qualitative data was expressed as percentage. Independent t test was used for comparing quantitative data between two groups.

Analysis was done to compare relation of age, BMI, gravida and blood pressure in GDM and normal pregnancy.

RESULTS

The present study on factors associated with gestational diabetes mellitus was conducted in a total of 200 subjects divided into two groups. One of the groups comprised of 50 women with GDM and the other included 150 normal pregnant controls. Maternal age, BMI, gravida and blood pressure were included as the baseline parameters.

Age (Years)	GDM	Controls
Mean	26.24	23.77
SD	4.44	3.51

Table 1. Age of the Study Population

p value <0.01

The mean age in women with GDM was found to be 26.24 years and that in controls was 23.77 years. The difference was statistically significant with a p value <0.01. Onset of GDM was found in women of earlier age in the present study group.

Body Mass Index (Kg/m2)	GDM	Controls
Mean	26.98	23.42
SD	1.54	1.64

Table 2. Body Mass Index of Women with GDM and Normal Pregnant Women

p value <0.001

The mean value of Body Mass Index of women with GDM was 26.98 Kg/m^2 and that in normal pregnant women was 23.42 Kg/m^2. The p value was <0.001 (highly significant). In the present study, women with GDM were found to have overweight and controls are found to have normal weight.

Age in years	Primi	Gravida 2	Gravida 3	Gravida 4
GDM	24.1	25.8	28.3	29.7
SD	5.3	2.8	2.8	0.5
Control	22.3	24.8	25.9	24.9
SD	3.1	3.3	2.90	4.10

Table 3. Mean Age in GDM and Control Groups in Relation to Gravida

The mean age in GDM and normal pregnant women was compared. In GDM, primi had a mean age of 24.1 years while in normal pregnancy it was 22.3 years.

Weight in Kg	Primi	Gravida 2	Gravida 3	Gravida 4
GDM	65.4	64.1	60.0	70.0
SD	7.6	2.09	7.3	9.2
CONTROL	56.6	57.5	58.7	60.3
SD	4.4	4.5	6.10	6.30

Table 4. Mean Weight in GDM and Control Groups in Relation to Gravida

No significant relation was observed between gravida and occurrence of GDM. This may be due to the fact that

gravida and parity are not directly linked to insulin sensitivity though these factors may be linked to progressive ageing and increase in body weight.

Systolic Blood Pressure (mm of Hg)		
	GDM	Controls
Mean	122.04	113.17
SD	9.53	4.65
Table 5a. Comparison of Systolic Blood Pressure of Women with GDM and Normal Pregnant Controls		
p value <0.01		

Diastolic Blood Pressure (mm of Hg)		
	GDM	Controls
Mean	79.76	73.13
SD	7.81	3.51
Table 5b. Comparison of Diastolic Blood Pressure of Women with GDM and Normal Pregnant Controls		
p value <0.01		

The mean systolic blood pressure in women with GDM was 122.04 mm of Hg and that in pregnant controls was 113.17 mm of Hg (p value < 0.01, significant). The mean diastolic blood pressure in women with GDM was 79.76 mm of Hg and that in pregnant controls was 73.13 mm of Hg and the result was significant.

DISCUSSION

The mean age of the GDM group in the present study was found to be 26.24 years and was significantly higher than that of controls with a mean of 23.77 years. This is in accordance with the Fourth International Workshop Conference on GDM which recommended a screening strategy based on risk assessment and considered age less than 25 years as a low risk group.[1] The mean age of occurrence of GDM, according to the present work, is lower than that observed in other populations.[2,3] Hill et al in a study conducted in South India observed a mean maternal age of 23.6 years in women with GDM.[4] The occurrence of diabetes in Indians was found to be 10 to 15 years earlier than in western population in a study comparing the two.[5] The UK Prospective Diabetes Study concluded that Asians develop type 2 diabetes earlier than Afro-Caribbean and White Caucasians.[6]

Body Mass Index is a factor highly implicated in the pathogenesis of gestational diabetes. According to the World Health Organization, obesity is defined as BMI ≥30 Kg/m^2, overweight category includes BMI 25-29.9 Kg/m^2 and normal weight is BMI 18-24.9 kg/m^2. The mean BMI of GDM women in the present work was found to be 26.98 Kg/m^2, significantly higher than 23.42 Kg/m^2 in controls. Though this BMI does not fit into the obese category, overweight was found to be associated with GDM. The prevalence of obesity in Southeastern Asian women is only 0.9% according to National Institute of Health Standards.[7] It has been suggested that specific BMI classifications should be validated for Asian women.[8] A mean BMI of 23.1 Kg/m^2 was observed in women with GDM in a study conducted in India.[4] The DECODE-DECODA Study Group on behalf of the European Diabetes Epidemiology Group and the International Diabetes Epidemiology Group found that the prevalence of diabetes in Indians starts increasing at a lower BMI compared to Chinese, Japanese and Europeans.[9] Indians, having a very high prevalence of type 2 diabetes were found to have significantly lower incidence of obesity compared to Caucasians. The difference in the degree of insulin resistance contributing to increased incidence of type 2 diabetes in Indians may be explained by either an environmental or genetic factor or a combination of both.[5] The possible role of genetic factors in Indians has been studied by several investigators.[10,11] Studies have shown an association with plasma cell membrane glycoprotein PC-1 121 Q variant and genes involved in β cell growth, survival, insulin secretion and action. The role of the brain in glucose homeostasis and the mechanism linking obesity to type 2 diabetes has also been implicated. A whole genome association study followed by analysis can lead to a conclusion about genes involved and the mode of their interactions in GDM and type 2 diabetes in Indians.

A longitudinal study by Damm on GDM and subsequent diabetes concluded that even non-obese women with previous GDM are characterized by the metabolic profile of NIDDM-insulin resistance and impaired insulin secretion.[12] This indicates the importance of lifestyle intervention and regular assessment to prevent or delay development of diabetes or detect diabetes if it develops. The biggest risk factor is a GDM pregnancy and BMI is a factor which may influence the development of diabetes in women with GDM.[7]

GDM is associated with higher than expected rate of obesity as well as impaired glucose tolerance in children and young adults who were exposed to hyperglycaemia in utero. Silverman et al reported that offspring of diabetic mothers had increased chance of childhood obesity and lower neuropsychological development.[13] Studies of chemically-induced diabetes in rodent models have revealed important defects in insulin action and β cell functions in adult animals that have been exposed to a diabetic intrauterine environment.[14] Although the relative contributions of genetics and the intrauterine environment to the same problem in humans are still being studied, at least some environmental components seem to be operative. Pettit and colleagues observed higher rates of obesity and higher blood glucose levels in offspring exposed to diabetes in utero, compared with their siblings who were born before their mother had developed diabetes.[15] Gillman et al examined the effect of GDM on adolescent BMI and found an association between the two.[16] Hill et al also had similar observations.[4] Lee et al have found that BMI of offspring of GDM mothers, more than or equal to 5 years of age, was significantly higher and these children had early manifestations of cardiovascular risk factors.[17] Grace et al in a study on birth characteristics of women who later developed diabetes observed that women whose mothers had had diabetes during pregnancy were at increased risk of gestational diabetes.[18] According to Hod proliferation of foetal adipocytes, muscle cells, pancreatic β cells and

neuroendocrine systems is the basis for the development of obesity or type 2 diabetes in later life.[19]

According to Metzger and Coustan obesity is a factor associated with increased risk of progression to diabetes within 5 years of GDM.[20] Sheshiah et al observed a linear increase in the prevalence of GDM with increasing BMI in a study conducted in India.[21] Obesity was recognized as a high risk factor necessitating early testing of glucose intolerance by the Organizing Committee of the Fourth International Conference on GDM.[19] Naylor et al developed a selective screening approach instead of the previously recommended universal screening for diagnosis of GDM.[22] BMI was one of the factors on which the scoring system for categorization of women into low, intermediate and high risk groups was based. This approach resulted in a 34.6% reduction in the number of screening tests performed without any decrease in the detection rate of GDM. The ADA now recommends selective screening for GDM and obesity is considered to be a high-risk factor.[23] A prospective cohort study conducted in Iran to determine incidence and complications of GDM identified obesity as a risk factor.[2]

Apart from increasing the risk of GDM, obesity is an independent predictor of foetal weight and macrosomia.[22] Ramachandran et al conducted a study on foetal outcomes in GDM in Indians.[24] The study concluded that increasing BMI was an independent risk factor for having big babies in addition to elevated blood glucose levels. Langer studied the impact of increased BMI on pregnancy outcome and concluded that insulin was required for a good outcome in obese women.[25] Moore has also documented that birth weight is determined by factors other than hyperglycaemia, the most significant being pre-pregnancy BMI.[26] Graf concluded that maternal obesity was a strong risk factor for macrosomia throughout pregnancies with GDM while maternal glucose values had association restricted to 32 to 35 weeks.[27] In obese women the high foetal macrosomia could not be normalized by therapy based on maternal euglycemia. This finding points to the importance of maintaining normal BMI. Maternal BMI was found to be a predictor of foetal weight and BMI of offspring at follow up.[22]

Obesity itself causes some degree of insulin resistance. A prospective longitudinal study on glucose metabolism in obese women with GDM by Catalano et al concluded that obese gestational diabetics had greater insulin resistance compared to normal weight women with GDM.[28] Increased BMI associated with GDM leads to a state of insulin resistance additive to insulin resistance of GDM. Of all factors associated with GDM, obesity is a modifiable factor to a certain extent as documented by the results of large studies on prevention of diabetes in future in women with GDM.[29] Several mechanisms have been suggested for the increased insulin resistance in obese women with GDM. Increased intramyocellular lipid concentration was found to occur in women with previous GDM and is considered as a parameter of insulin resistance that predicts type 2 diabetes according to Willer et al.[30] Plasma FFA resulting from dietary fat supply and or increased lipolysis in fat tissue may directly induce insulin resistance or could be channelled preferentially into triglycerides. Increased FFA uptake or lipolysis of intramyocellular lipid can inhibit insulin action via decreased IRS-1 phosphorylation. Catalano et al observed down regulation of IRS-1 and PPAR-γ in obese gestational diabetics more than that in GDM.[31] The central role of maternal obesity in GDM was investigated in detail by Retnakaran et al.[32] A cross sectional study was conducted in pregnant women to determine whether CRP and other markers of subclinical information are elevated in GDM. BMI was found to correlate with CRP concentrations more than glucose tolerance status. Elevated CRP levels are found in type 2 diabetes as well. This suggests a model in which obesity mediates a systemic inflammatory response, with possible downstream metabolic sequelae, including insulin resistance and glucose dysregulation.

Categorization of GDM patients on the basis of factors including BMI can also aid in clinical management. Lean patients are less likely to be insulin resistant than overweight and obese, so that autoimmune diabetes should be considered in them. This warrants screening for evolving autoimmune diabetes by measuring antibodies especially in patients with no family history and belonging to ethnic groups in which type 1 diabetes is common.[1, 23] These patients require careful glucose level monitoring because they rapidly develop diabetes after pregnancy. For ethnic groups more prone to type 1 diabetes, GAD antibody may be measured. Genotyping for monogenic diabetes is still a research tool but clinical tests are being developed and are important for genetic counselling.[33] This is likely to have an important impact on population health.

An increased incidence of GDM in relation to gravida and parity has been documented in several studies. The present study revealed no significant relation between these factors and GDM. This result is similar to that obtained in a study conducted to analyse the effect of parity on impairment of insulin sensitivity and risk of GDM.[34] The study concluded that parity is not directly linked to insulin sensitivity although it is linked through progressive ageing and weight gain when there is a sufficiently long time interval between pregnancies. Obese women are more likely to have impaired glucose tolerance in subsequent pregnancies according to Philipson and Super.[35]

A significant increase of GDM in relation to gravida was noted in a study conducted by Sheshiah et al.[21] Parity is a factor associated with increased incidence of GDM according to Metzger and Coustan.[20] A prospective study conducted in Columbia University and a retrospective study in Singapore revealed similar results.[36] The effect of parity on impairment of insulin sensitivity during pregnancy and on risk of GDM was studied and a significant relation was observed. Recurrence of gestational diabetes in subsequent pregnancies was documented in 20 of 30 pregnancies by Philipson and Super.[35] Obese women were more likely to have this effect.

The precise reason for pregnancy induced hypertension associated with GDM is unknown. It is probably related to insulin resistance and is observed even in the absence of vascular complications. Treatment of insulin resistance,

therefore results in reduced incidence of this complication. A link with glycaemic control has been suggested by several studies.[26] The present study revealed significantly higher systolic and diastolic pressures in GDM compared to controls though these values are within normal limits.

CONCLUSIONS

GDM women were found to be overweight when compared to the control group. Status of gravid was found to have no significant relation with GDM. Blood pressure was significantly higher in GDM women even though it was within the normal range.

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REFERENCES

[1] Buchanan TA, Xiang AH. Gestational diabetes mellitus. J Clin Invest 2005;115(3):485-491.
[2] Keshavarz M, Cheung WN, Gholam Reza Babaee RG, et al. Gestational diabetes in Iran: incidence, risk factors and pregnancy outcomes. Diab Res Clin Pract 2005;69(3):279-286.
[3] Yogev Y, Xenakis EMJ, Langer O. The association between preeclampsia and the severity of gestational diabetes: the impact of glycemic control. Am J Obstet Gynecol 2004;191(5):1655-1660.
[4] Hill JC, Krishnaveni GV, Annamma I, et al. Glucose tolerance in pregnancy in South India: relationships to neonatal anthropometry. Acta Obstet Gynecol Scand 2005;84(2):159-165.
[5] Das SK. Genetic epidemiology of adult onset Type 2 Diabetes in Asian Indian population: past, present and future. Int J Hum Genet 2006;6(1):1-13.
[6] UK Prospective Diabetes study. XII: differences between Asian, Afro-Caribbean and white Caucasian Type 2 diabetic patients at a diagnosis of diabetes. UK Prospective Diabetes Study Group. Diabet Med 1994;11(7):670-677.
[7] Kitzmiller JL, Dang – Kilduff L, Taslimi MM. Gestational diabetes after delivery - short-term management and long term risks. Diabetes Care 2007;(30 Suppl 2):S225-A235.
[8] Snehalatha C, Viswanathan V, Ramachandran A. Cutoff values for normal anthropometric variables in Asian Indian adults. Diabetes Care 2003;26(5):1380-1384.
[9] Nakagami T, Qiao Q, Carstensen B, et al. DECODE-DECODA Study Group. Age, body mass index and type 2 diabetes – associations modified by ethnicity. Diabetologia 2001;46(8):1063-1070.
[10] Abate N, Carulli L, Cabo-Chan Jr A, et al. Genetic polymorphism PC–K121Q and ethnic susceptibily to insulin resistance. J Clin Endocrinol Metab 2003;88(12):5927-5934.
[11] Mohan V, Vimaleswaran KS, Anjana M. The Thr 394 Thr (G-A) polymorphism of PGC-1α gene is associated with visceral fat and Type 2 Diabetes in Asian Indians. American Diabetes Association Annual Meeting 2005: p. 1174.
[12] Damm P. Gestational diabetes mellitus and subsequent development of overt diabetes mellitus. Dan Med Bull 1998;45(5):495-509.
[13] Silverman BL, Rizzo TA, Green OC, et al. Long term prospective evaluation of offspring of diabetic mothers. Diabetes 1991;(2):121-125.
[14] Buchanan TA, Kjos SL. Gestational diabetes: risk or myth? The J Clin Endocrin and Metab 1999;84(6):1854-1857.
[15] Pettitt DJ, Knowler WC. Long term effects of the intra uterine environment, birthweight and breast-feeding on Pima Indians. Diabetes Care 1998;(21 Suppl 2):B138-B141.
[16] Gillmann MW, Rifas-Shiman S, Berkey CS, et al. Maternal gestational diabetes, birth weight and adolescent obesity. Pediatrics 2003;111(3):e221-e226.
[17] Lee H, Jang HC, Park HK, et al. Early manifestation of cardiovascular risk factors in offspring of mothers with previous history of gestational diabetes mellitus. Diabetes Res Clin Pract 2007;78(2):238-245.
[18] Egeland GM, Skjaervan R, Irgans LM. Birth characteristics of women who develop gestational diabetes: population based study. BMJ 2000;321(7260):546-547.
[19] Hod M. Gestational diabetes mellitus: past, present and future. Diabetes Rev 1998;5:603-612.
[20] Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop - Conference on Gestational Diabetes Mellitus. Diabetes care 1998;21(Suppl 2):B161-B167.
[21] Seshiah V, Balaji V, Balaji MS, et al. Gestational diabetes mellitus in India. J Assoc Physician India 2004;52:707-711.
[22] Naylor CD, Sermer M, Chen D, et al. Selective screening for gestational diabetes mellitus. Toronto Trihospital Gestational Diabetes Project Investigators. N Engl J Med 1997;337(22):1591-1596.
[23] American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2004;27(Suppl 1):S5-S10.
[24] Ramachandran A, Snehalatha C, Clementina M, et al. Foetal outcome in gestational diabetics in South Indians. Diabetes Research and Clinical Practice 1998;41(3):185-189.

[25] Langer O, Conway DI, Berklus MD, et al. A comparison of Glyburide and insulin in women with gestational diabetes mellitus. The New England Journal of Medicine 2000;343(16):1134-1138.
[26] Moore TR. Diabetes mellitus and pregnancy. Diabetes mellitus and pregnancy excerpt. Section 2, Jan 27, 2005.
[27] Schaefer UM, Songster G, Xiang A, et al. Congenital malformations in offspring of women with hyperglycemia first detected during pregnancy. American Journal of Obstet and Gynecol 1997;177(5):1165-1171.
[28] Catalano PM, Huston L, Amini SB, et al. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. Am J Obstet Gynecol 1999;180(4):903-916.
[29] Buchanan TA, Metzger BE, Freinkel N, et al. Insulin sensitivity and β - cell responsiveness to glucose during late pregnancy in lean and moderately obese women with normal glucose tolerance or mild gestational diabetes. Am J Obstet Gynecol 1990;162(4):1008-1014.
[30] Kautzky-Willer A, Krssak M, Winzer C, et al. Increased intramyocellular lipid concentration identifies impaired glucose metabolism in women with previous gestational diabetes. Diabetes 2003;52(2):244-251.
[31] Catalano PM, Nizelski SE, Shao J, et al. Down regulated IRS-1 and PPAR-γ in obese women with gestational diabetes: relationship to FFA during pregnancy. Am J Physiol Endocrin Metab 2002;282(3):E522-E533.
[32] Retnakaran R, Hanley AJG, Raif N, et al. C-reactive protein and gestational diabetes: The central role of maternal obesity. The J Clin Endocrin and Metab 2003;88(8):3507-3512.
[33] Fajans SS, Bell GI, Polonsky KS. Molecular Mechanisms and clinical pathophysiology of maturity onset diabetes of the young. N Eng J Med 2001;345(13):971-980.
[34] Seghieri G, De Belly A, Anichini R, et al. Does Parity increase insulin resistance during pregnancy? Diabet Med 2005;22(11):1574-1580.
[35] Cunningham FG, Gant NF, Levino KJ, et al. Diabetes. Williams Obstetrics. Vol. 8. 21st edn. New York: McGraw-Hill Publication 2001: p. 173-175, 1359-13281.
[36] Kabiru W, Raynor DB. Obstetric outcomes associated with increase in BMI category during pregnancy. Am J Obstet Gynecol 2004;191(3):928-932.