

Gestational Diabetes Mellitus Diagnosed with 2hr 75g- Oral Glucose Tolerance Test (D.I.P.S.I) and Its Adverse Perinatal Outcome

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Research Article

Abstract: Objective: The aim of the study was to assess the maternal and fetal complications of pregnancy in mothers with gestational diabetes mellitus compared with non-diabetic mothers.

Method: A Prospective cohort study of 1000 consecutive non-selected pregnancies who came to Krishna Hospital for routine antenatal screening in the year 2011-2013. Diagnosis of Gestational diabetes mellitus was done by single step screening -75gms glucose OGTT(ORAL GLUCOSE TOLERANCE TEST) suggested by D.I.P.S.I. The outcome of pregnancy in 220 patients (22%) with gestational diabetes identified and matched for age, parity, body mass index with 220 non-diabetic controls were studied retrospectively from case files. **Results:** The G.D.M patients were treated with either diet alone (M.N.T) or with additional insulin in some patients who required for better control of their blood sugar levels. Patients with G.D.M had a significantly higher incidence of pre-eclampsia(38% p<0.001); preterm delivery (18% p=0.0226); induction of labour(15% p<0.001); caesarean section (60% p =0.003);higher mean birth weight of babies(3.335+-0.5 p<0.001); macrosomia (30% p=0.0186) and admission to the neonatal intensive care unit (16% p=0.003) compared with the control group. The rates of apgar score <7 at 5 mins, respiratory distress syndrome, neonatal hypoglycemia, hyperbilirubinemia and the need for phototherapy were higher in G.D.M patients. Congenital anomaly and perinatal mortality rates were not significantly different in the two groups. Women with early diagnosis of gestational diabetes mellitus had a significantly increased need for insulin treatment during pregnancy (36% versus 9% p<0.005) and a significantly higher occurrence of diabetes mellitus at follow up from two months. **Conclusions:** G.D.M is recognised to be associated with increased rates of adverse maternal and neonatal outcomes which are supported by the findings of this study. Even the mild forms of G.D.M. seem to have significant consequences for women and their offspring's and it's recommended to treat them aggressively. Evidence suggests early diagnosis and strict control of blood sugar level throughout the pregnancy can significantly reduce maternal and fetal complications.

Keywords: gestational diabetes mellitus, pregnancy, DIPSI, Prevalence.

Introduction

Gestational Diabetes Mellitus (G.D.M), is defined as carbohydrate intolerance diagnosed for the first time during pregnancy¹. The **prevalence** of GDM ranges from

1 to 14% depending on different screening methods, diagnostic criteria and the population screened. The incidence of diabetes complicating pregnancy has increased approximately 40 % between 1989 and 2004(GETAHUN AND COLLEAGES 2008). As the incidence of diabetes is rising in epidemic proportion, more women of child bearing age are at increased risk of diabetes during pregnancy¹.Infact, a high prevalence of gestational diabetes around 18% has been reported in India² This condition has been implicated as a risk factor for future diabetes and obesity in women as well as for impaired carbohydrate metabolism in their offspring³. Recently the effect of screening and clinical management of GDM on antenatal ,neonatal and perinatal outcome has been deemed beneficial⁴.The purpose of screening , treatment and management of GDM is twofold ; to prevent stillbirths and too decrease the number of large for gestational age birth ,ultimately reducing neonatal and maternal morbidity and mortality⁵. Although still birth rates have decreased dramatically over the last 20yrs, the rates of Caesarean section and of large for gestational age birth weight have remained high and in some cases are unchanged among women with GDM despite of introduction of insulin therapy⁵⁻⁶.

Materials and Methods

A **retrospective cohort study** conducted on 220 patients with GDM who were diagnosed and treated at Krishna Institute of Medical Sciences, Karad between July 2011 and July 2013. Antenatal and perinatal data obtained from the patient's medical records and hospital database included: age, parity, BMI, gestational age at delivery, antenatal complications, mode of delivery, and birth weight of the baby, as well as maternal and neonatal morbidity and mortality. The control group consisted of 220 non-diabetic pregnant women were randomly selected from the obstetric patients that matched for age, parity and BMI, who delivered in the hospital during the

study period. Women who had multiple pregnancies and breech presentation in labor were excluded from the analysis. The neonatal outcomes included: birth weight at delivery; respiratory distress syndrome (RDS); hypoglycemia (<45 mg/dL); hypocalcemia (<9 mg/dL); hyperbilirubinemia (<12 mg/dL; these levels apply to term babies); and neonatal intensive care unit (NICU) admission for >24 hours. Apgar scores at 1, 5 and 10 minutes were noted from the delivery records. Neonates with jaundice (serum bilirubin ≥ 12 g/dL) were treated with phototherapy. The pregnant women attending the antenatal clinics during the study period were tested for GDM by a universal screening procedure and following risk factors were noted: age ≥ 30 years; 20% pre-pregnancy overweight; family history of diabetes mellitus; GDM in a previous pregnancy; previous unexplained stillbirth or neonatal death; previous delivery of a macrosomic baby (birth weight >4 kg); and glycosuria in ≥ 2 antenatal visits.

DIPSI Recommended Method

The single step of 75gm oral glucose tolerance test is used for both screening and diagnosis

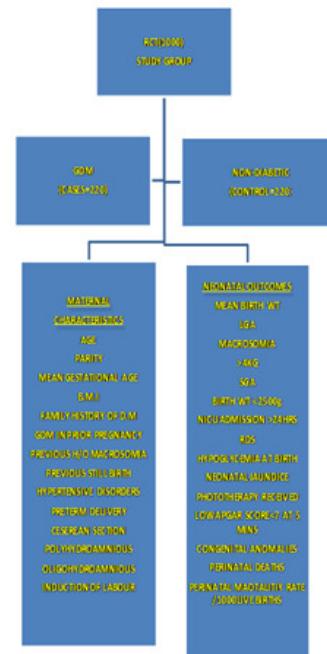
As a pregnant woman walks into to antenatal clinic, she has to be given a 75gm oral glucose load and at 2hrs a venous blood sample is collected for estimating plasma glucose. This one step procedure of challenging women with 75gm glucose and **diagnosing GDM is simple, economical, and feasible.**

In Pregnancy	Outside	Pregnancy
2hr > 200 mg/dl	DIABETES	DIABETES
2hr > 140mg/dl	GDM	IGT
2hr > 120 mg/dl	DGTT	-----

Gestational Week at Which Screening is Recommended

The fetal beta cells recognizes and responds to maternal glycemic level as early as 16th week of gestation .The usual recommendation for screening is between 24 and 28 weeks of gestation. The recent concept is to screen for glucose intolerance in the first trimester itself as the fetal beta cells recognizes and responds to maternal glycemic level as early as 16th week of gestation. If found negative at this time, the screening test is to be performed again around 24th-28th week and finally around 32-34 week.

Maternal and Neonatal Characteristics That Were Studied



Patients diagnosed to have GDM were put on an 1800-kcal diabetic diet for 5 days followed by a blood sugar profile (BSP) to measure the fasting blood sugar and 2-hrs postprandial-breakfast, lunch and dinner serum glucose levels. If the fasting blood sugar was ≤ 100 mg/dL and the postprandial blood sugar levels <125 mg/dL; the patients were managed by diet alone. Patients with higher values were treated with subcutaneous injections of regular and NPH insulin, twice daily (half an hour before breakfast and dinner). Control of blood sugar levels was monitored by bi-weekly BSP. There were 171 GDM patients treated with the diabetic diet alone, and 49 required additional insulin, besides the diet. The patients were seen every two weeks and USG examinations were performed every 4 weeks from the time of diagnosis. Labor was induced at 40 weeks in the GDM patients controlled on diet alone without any pregnancy complication, if spontaneous onset had not occurred. Some patients required earlier induction of labor due to pre-eclamptic toxemia and poor biophysical profile. Blood sugar was measured in the newborns of diabetic mothers 30 minutes after delivery. In cases of hypoglycemia, measurements were repeated every two hours until stable values of ≥ 2.5 mmol were obtained. The hypoglycemic babies were treated with intravenous infusion of glucose, and breast feeding or formula was initiated as early as possible. In the control group, blood glucose was measured only when indicated by the clinical condition of the newborn. Statistical analysis was performed by a commercial package program (SPSS 17, Chicago, Illinois). Chi-square test was performed to assess the statistical significance by the Fisher's exact

test. Odds ratio (OR) and 95% confidence intervals (CI) were calculated. All p values were two-tailed and values of ≤ 0.05 were considered significant. The results are given as mean \pm standard deviation (SD) for normally distributed data and as frequencies (n) and percentages (%) for nominal data. To assess the independent effect of the risk factors attributing to GDM and to evaluate the independent effect of GDM on the maternal and neonatal outcomes; multivariate logistic regression was used to estimate adjusted OR and CI. The model included the significant variables found. Statistical analysis was performed using SPSS 16 (SPSS Inc, Chicago, IL). The study was approved by the hospital Health Research and Ethics review board.

Results

Among the 1000 deliveries that occurred during the period of study, 220 (22%) of them were complicated with GDM. The demography and pregnancy outcome of women in the two groups are presented in Table. The mean gestational age at delivery was significantly different in the two groups of patients, as was history of GDM in a previous pregnancy. Statistically significant differences in pregnancy complications between the study patients and control noted were: hypertensive disorders ($p<0.0001$); preterm delivery ($p=0.0226$); induction of labor ($p<0.0001$); and CS rate (24.1% vs. 12.3%; $p<0.0019$), which were also high risk variables found on multivariate logistic regression. After the adjustment for confounders, multivariate logistic analysis finally indicated that women who had a history of GDM in the previous pregnancies were at higher risk of having GDM. The neonatal outcomes are shown in Table. Neonates born to women with GDM had a significantly higher mean birth weight than babies born of mothers from the control group ($p<0.0001$); the neonates were also large for gestational age (LGA) babies ($p=0.0011$) and macrosomic (birth weight ≥ 4000 g) compared with the neonates born to mothers from the control group. Approximately 16.4% of babies delivered by GDM mothers were admitted to the NICU for >24 hours compared to 5.5% in the control group ($p=0.0003$). After adjusting for potential confounding variables as listed in Table 1; infants born to mothers with GDM were at higher risk of macrosomia or being large for gestational age (Table 2). The incidence of neonatal congenital anomalies and perinatal mortality rate was similar to the controls. There was no difference in the rates of maternal and neonatal complications (including neonatal macrosomia) in GDM mothers treated with and without insulin.

Discussion

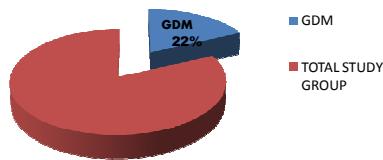
GDM has been recognized as a clinical entity for the past 50 years⁵. It is associated with a high risk of type 2 diabetes mellitus developing in the patients later on in life, depending on the ethnicity and length of follow-up.^{6,9} Early studies have strongly indicated untreated carbohydrate intolerance during pregnancy to be associated with higher rates of maternal morbidity and perinatal morbidity and mortality^{10,12}. The purpose of screening, treatment and management of GDM is to prevent stillbirth, and decrease the incidence of LGA babies, thereby reducing maternal and perinatal morbidity and mortality. The occurrence of LGA babies is not necessarily attributable to abnormal glycemic control. Maternal age, parity, ethnicity and obesity along with fetal hyperglycemia are possible contributory risk factors for excessive fetal growth^{13,14}. The findings of the present study conform to those of other studies reported in the literature, that GDM patients are liable to have adverse pregnancy outcomes.^{3,16-18} As expected, women with GDM in the present study were found to have a higher proportion of obstetric complications including pre-eclampsia, preterm labor and CS, as well as mean birth weight, LGA and macrosomic babies than the controls. High rates of labor induction (33-38%) among GDM patients have been reported by other authors in the past^{19,20} which reflect the findings in this study (31.8%). The common indications for induction in this study were pre-eclampsia; undelivered at 40 weeks gestation controlled on diet alone, with no complication; patients who required insulin intervention; premature rupture of membranes; and maternal-related causes. Many studies have found high caesarean delivery rates in GDM patients despite good maternal blood glucose control during pregnancy^{3,5,15,17,19}. The significantly higher rate of CS in the GDM patients compared to the controls, reflect the findings of this study. The main indications for CS in this study were maternal hypertension, macrosomia, non-reassuring fetal heart tracing, failure to progress and previous history of caesarean sections. The significantly higher CS rates in the GDM patients than the controls conform to this study. The CS rate of 24.1% in this series correlates with 19-30% reported in previous studies,^{18,20,21} but lower than 32.9-41.4% found in some reports.^{3,5,15}. The higher labor induction rate in the GDM patients may have had a small contribution to the increased caesarean deliveries in this series; although the caesarean section rate is not unusually high compared with other reports in the literature. Some authors have reported that serious perinatal morbidity can be reduced with treatment of the mothers with GDM^{15, 16, 17}. Published, randomized clinical trials confirm that treating pregnant patients with even the mildest form of GDM can reduce the risk of

common birth complications among the infants and blood pressure disorders in the mothers^{22, 23}. The rate of pregnancy complications in the study was similar among the GDM patients treated with diet alone and those who received additional insulin alongside the diet, which correlated with the findings of some reports^{15,21}. Significantly higher rates of preterm delivery and admission of babies to the NICU have been reported in the GDM patients treated with insulin and diet compared with those on diet alone,^{16,24} which were contrary to the findings in this and other series^{3,5}. Many complications of pregnancy that are commonly associated with GDM such as polyhydramnios, oligohydramnios, SGA neonates, neonatal hypoglycemia and those requiring phototherapy were not significantly increased in the patient group of this study compared with the control. The incidence of 16.4% of neonates of GDM mothers admitted to the NICU in this study was significantly higher than the control ($p<0.0003$). Although, the Apgar scores were not strikingly different between the two groups studied; babies born to GDM mothers spent significantly more time in the NICU than babies born to mothers from the control group. This may reflect the routine policy of

observation of these infants at the hospital where this study was based and not necessarily associated with any medical problems. In GDM, increased numbers of pregnancy risk factors and fetal complications appear to cause significant numbers of NICU admissions >24 hours. The rate of NICU admission (16.4%) in the study for GDM neonates was lower than 28.7% reported in one study.¹⁸ Some studies concluded that even very mild alterations in glucose tolerance can result in abnormal fetal growth which can be prevented by simple but aggressive control of blood sugars in order to ameliorate many of the complications for the mother and the baby^{22, 23}. Dietary intervention and insulin therapy, with their safety profile, have been considered the gold standard of pharmacotherapy for GDM. On the other hand, a number of trials, including prospective randomized trials, have demonstrated the efficacy of oral hypoglycemic agents, particularly glyburide and metformin, used in managing pregnant diabetics²⁴. Furthermore, a short-term study has not shown any adverse effect of these oral medications on the fetus, which are increasingly being used in pregnancy²⁵.

Incidence of GDM by Considering DIPSI Recommended Method

Among the 1000 deliveries that occurred during the period of study, 220 (22%) of them were complicated with GDM.

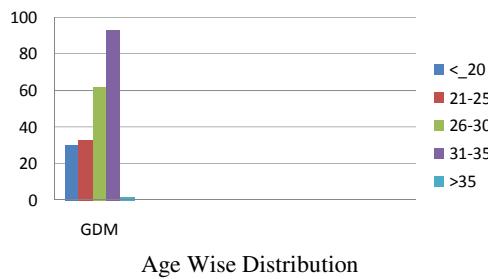


Study	Incidence
V.Seshaih	17.7%
Vanita Das Et Al	4%
Mamta Bhat Et Al (Chennai Study)	9%
Kevin Johns Et Al (Canada Study)	3-10%
Fakhlaghi Et Al (Iran Study)	3-5%
J.G. Ray At Al (Deposit Study)	11%
Banaerjee Et Al (Kolkata Study)	3-5%
Perzent Study	22%

Prevalence of GDM (Considering DIPSI)

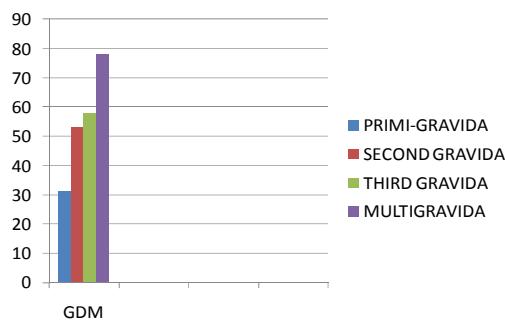
QTY	Prevalence %
Trivendrum	15%
Alwaye	21%
Banglore	12%
Erode	18%
Ludhiana	17.5%

Maternal Characteristics and Pregnancy Outcomes in GDM



Age Wise Distribution

- The mean gestational age of patients with gdm: 29.4+/-7.5 yrs
- The prevalence proportion increased from 14.5% in age group of 15-19 yrs to 28 % in the age group >30yrs. (linear trend was statistically significant (p<0.05)



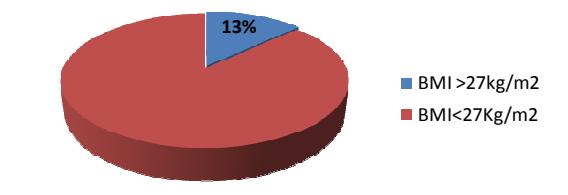
Gravidity of Patients with GDM

Prevalence of GDM Increases by Gravidity from 16.3% in Primigravidae to 25.8% In Gravidas >_4

Mean Gestational Age at Delivery

Characteristic	GDM n=220	Control N=220	P Value	Or (95% CI)	Adjusted Or (95% CI)
Men Gestational Age at Delivery	38.6+/-1.4	39.4+/-1.6	0.0001*	0.082-0.518	0.101-0.645

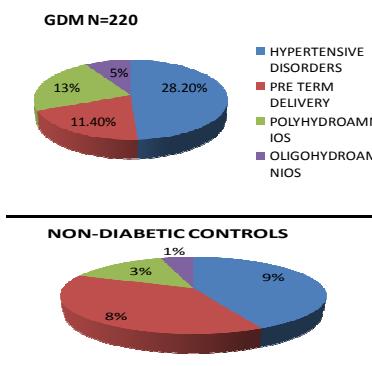
Obesity: Body Mass Index (B.M.I) :>27 Kg/m²



History

Characteristics	GDM N=220	Control N=220	P Value	Or (95% CI)	Adjusted Or (95% CI)
Family H/O Diabetes Melilitus	91 (41.4%)	71 (32.3%)	0.0602		
GDM in prior pregnancy	43 (19.5%)	17 (7.1%)	0.0004*	2.901 (1.597-5.268)	2.072 (1.064-4.745)
Previous History of Macrosom IC Baby	16 (7.3%)	10 (4.5%)	0.3121		
Previous Still Birth	3 (1.4%)	4 (1.8%)	1.000		

Maternal Complications



Maternal Complications	GDM (Cases) N=220	Non-Diabetic Control	P Value	Or (95% CI)	Adjusted Or (95%CI)
Hypertensive Disorder	62 (28.2%)	19 (9%)	<0.0001*	3.53 (1.834-6.824)	2.958 (1.251-6.313)
Preterm Delivery	25 (11.4%)	17 (8%)	0.0226*	2.435 (1.167-5.082)	2.012 (1.058-4.861)
Poly Hydramnios	27 (13%)	7 (3%)	0.338		
Oligo-Hydramnios	11 (5%)	2 (1%)	0.227		

Mode of Delivery

Mode of Delivery	GDM	Control	P Value	Or (95%CI)	Adjusted Or (95%CI)
Induction of Labour	70 (31.8%)	27 (12.3)	<0.0001*	2.072 (1.064-4.745)	3335 (2.038-5.459)
Caesarean Section	53 (24.1%)	27 (12.3%)	0.00019*	2.268 (1.365-3.768)	2.133.122-2.933)

- Higher rates of labour Induction among GDM patients have been reported by other studies 33-38% which reflects the findings in this study 31.8%.
- Common indications were pre-eclampsia, undelivered at 40 wks of gestation controlled by diet alone, with insulin interventions, prom and maternal related causes.
- Higher rates of caesarean section in GDM was confirmed in this study (24.1% correlates with 19-30% in other studies)
- Common indications were hypertension, macrosomia, non reactive NST, failure to progress and previous history of caesarean sections.

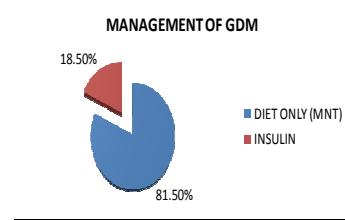
Study

Study	Incidence of LSCS
Martin et al (1987)	50%
Kitzmiller et al (1978)	69%
Schneider et al (1980)	70%
Leveno et al (1979)	81%
Canada Study Kevin Johns et al (2001)	36.3%
K Kuh Study Malak M. Alhakeem et al (2006)	21%

Treatment Received

Out of all 220 gestational diabetes patient only 41(18.5%) patients required insulin therapy. rest 179 (81.5%) patients maintained basal sugar levels within normal limits with dietary modifications only (medical nutritional therapy).

HbA1c level in gestational diabetic cases were in the range of 7-8%



Neonatal Outcomes

Neonatal Outcome	GDM	Non-Diabetic Controls	P Value	Or (95%CI)	Adjusted OR (95%CI)
Mean Birth WT (gm)	3545+/-466	3356+/-332	<0.0001*	(113.18-264.82)	(105-231.40)
Over all GA	32 (14.5)	11 (5.0)	0.0011*	3.234 (1,585-6.396)	3.341 (1.464-6.375)
Macro SOMIA	28 (12.7)	11 (5.0)	0.0186*	2.77 (1.342-5.717)	2.67 (1.232-5.514)
SGA	16 (7.3)	15 (6.8)	1.000		
Birth Weight <2500gm	8 (3.6)	7 (3.2)	1.000		

- The purpose of screening, treatment and management of GDM is to prevent still birth and decrease the incidence of LGA babies, thereby reducing maternal and perinatal morbidity and mortality.
- The occurrence of LGA is not necessarily attributable to abnormal glycemic control.
- Maternal age, Parity, Ethnicity and Obesity along with fetal hyperglycemia are possible risk factor for excessive growth

Neonatal Outcome	GDM	Non-Diabetic Controls	P Value
RDS	3 (1.4)	2 (0.9)	0.6233
Hypoglycemia at Birth	6 (2.7)	2 (0.9)	0.2846
Neonatal Jaundice	18 (8.2)	10 (4.5)	0.1707
Phototherapy Required	11(5.0)	6 (2.7)	0.2017
Congenital Anomalies	3 (1.4)	2 (1.1)	1.0000

NICU Admissions >24 Hrs:

- The total NICU admissions were 36 (16.80%) out of 220 GDM patients in comparison to 5.5% in NON DIABETIC CONTROLS. (SIGNIFICANT P VALUE <0.0003)
- Reason:** increased number of pregnancy risk factor and fetal complications still birth:

GDM Cases 1

Non -Diabetic 0

Control

Difficulties During This Study

It was difficult to measure exact 75gm glucose. So it was made available as a premeasured commercial pack of 75gm amorphous glucose. It was difficult to calculate 2hours time after giving 75gm glucose for taking blood sample for individual separately ,so the patients were counselled to report back exactly after 2hours of consumption of glucose. The incidence of neonatal congenital anomalies was similar to the controls. There was no difference in the rates of maternal and neonatal complications (including neonatal macrosomia) in GDM mothers treated with and without insulin. But significantly higher rates of preterm delivery and admission of babies to the NICU in GDM cases treated with insulin compared with diet alone was observed.

Women with GDM in the present study were found to have a higher proportion of obstetric complications including pre-eclampsia, preterm labor and CS, as well as mean birth weight, LGA and macrosomic babies than the controls

Conclusion

The findings support the paradigm of increased rates of some maternal and neonatal complications in pregnant women with GDM ,BUT there is strong evidence which suggests that the reduction of complications can be significantly achieved by aggressive treatment of GDM.

References

1. Seshiah V, Balaji V, Balaji MS, Sanjeevi CB, Green A. Gestational Diabetes mellitus in India. J Assoc Physician India 2004;52:707-11.
2. Karcaaltincaba D, Kandemir O, Yalvac S, Guven S, Haberal A. Prevalence of gestational diabetes mellitus and gestational impaired glucose tolerance in pregnant women evaluated by National Diabetes Data Group and Carpenter and Coustan criteria. Int J Gynaecol Obstet 2009 Sep;106(3):246-249.
3. Sendag F, Terek MC, Itil IM, Oztekin K, Bilgin O. Maternal and perinatal outcomes in women with gestational diabetes mellitus as compared to nondiabetic controls. J Reprod Med 2001 Dec;46(12):1057-1062.
4. Reece EA. The fetal and maternal consequences of gestational diabetes mellitus. J Matern Fetal Neonatal Med 2010 Mar;23(3):199-203.
5. Jensen DM, Sørensen B, Feilberg-Jørgensen N, Westergaard JG, Beck-Nielsen H. Maternal and perinatal outcomes in 143 Danish women with gestational diabetes mellitus and 143 controls with a similar risk profile. Diabet Med 2000 Apr;17(4):281-286.
6. O'Sullivan JB. Diabetes mellitus after GDM. Diabetes 1991 Dec;40(Suppl 2):131-135.
7. Damm P, Kühl C, Bertelsen A, Mølsted-Pedersen L. Predictive factors for the development of diabetes in women with previous gestational diabetes mellitus. Am J Obstet Gynecol 1992 Sep;167(3):607-616.
8. Kjos SL, Peters RK, Xiang A, Henry OA, Montoro M, Buchanan TA. Predicting future diabetes in Latino women with gestational diabetes. Utility of early postpartum

glucose tolerance testing. *Diabetes* 1995 May;44(5):586-591.

9. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. *Diabetes Care* 2002 Oct;25(10):1862-1868.
10. Turok DK, Ratcliffe SD, Baxley EG. Management of gestational diabetes mellitus. *Am Fam Physician* 2003 Nov;68(9):1767-1772.
11. Reece EA, Homko C, Miodovnik M, Langer O. A consensus report of the Diabetes in Pregnancy Study Group of North America Conference, Little Rock, Arkansas, May 2002. *J MaternFetal Neonatal Med* 2002 Dec;12(6):362-364.
12. Langer O, Miodovnik M, Reece EA, Rosem BM. The proceedings of the diabetes in pregnancy study group of North America 2009 conference. *The J Matern-FetalNeonat Med* 2010; 23(3):196-198.
13. Casey BM, Lucas MJ, McIntire DD, Leveno KJ. Pregnancy outcomes in women with gestational diabetes compared with the general obstetric population. *ObstetGynecol* 1997 Dec;90(6):869-873.
14. Seghieri G, Anichini R, De Bellis A, Alyiggi L, Franconi F, Breschi MC. Relationship between gestational diabetes mellitus and low maternal birth weight. *Diabetes Care* 2002 Oct;25(10):1761-1765.
15. Johns K, Olynik C, Mase R, Kreisman S, Tildesley H. Gestational diabetes mellitus outcome in 394 patients. *J ObstetGynaecol Can* 2006 Feb;28(2):122-127.
16. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS; Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) Trial Group. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. *N Engl J Med* 2005 Jun;352(24):2477-2486.
17. Jimenez-Moleon JJ, Bueno-Cavanillas A, Luna-del-Castillo J, Gracia-Martin M, Lardelli-Claret P, Galves-Vargas R. Impact of different levels of carbohydrate intolerance on neonatal outcomes classically associated with gestational diabetes mellitus. *Eur J Obstet Gynecol Reprod Biol* 2001;102:36-41.
18. Ostlund I, Hanson U, Björklund A, Hjertberg R, Eva N, Nordlander E, et al. Maternal and fetal outcomes if gestational impaired glucose tolerance is not treated. *Diabetes Care* 2003 Jul;26(7):2107-2111.
19. Peticca P, Keely EJ, Walker MC, Yang Q, Bottomley J. Pregnancy outcomes in diabetes subtypes: how do they compare? A province-based study of Ontario, 2005-2006. *J ObstetGynaecol Can* 2009 Jun;31(6):487-496.
20. Tan PC, Ling LP, Omar SZ. The 50-g glucose challenge test and pregnancy outcome in a multiethnic Asian population at high risk for gestational diabetes. *Int J Gynaecol Obstet* 2009 Apr;105(1):50-55.
21. Xiong X, Saunders LD, Wang FL, Demianczuk NN. Gestational diabetes mellitus: prevalence, risk factors, maternal and infant outcomes. *Int J GynaecolObstet* 2001 Dec;75(3):221-228.
22. Bonomo M, Corica D, Mion E, Gonçalves D, Motta G, Meraati R, et al. Evaluating the therapeutic approach in pregnancies complicated by borderline glucose intolerance: a randomized clinical trial. *Diabet Med* 2005 Nov;22(11):1536-1541.
23. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al; Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. A multicenter, randomized trial of treatment for mild gestational diabetes. *N Engl J Med* 2009 Oct;361(14):1339-1348.
24. Paglia MJ, Coustan DR. The use of oral antidiabetic medications in gestational diabetes mellitus. *CurrDiab Rep* 2009 Aug;9(4):287-290.
25. Serlin DC, Lash RW. Diagnosis and management of gestational diabetes mellitus. *Am Fam Physician* 2009 Jul;80(1):57-62.