Research Article

Evaluation of the incidence and outcome of gestational diabetes mellitus using the current international consensus guidelines for diagnosing hyperglycaemia in pregnancy

Vinod G. Nair[1]*, Gurpreet S. Sandhu[2], Manash Biswas[3], Ritoo Bhalla[2]

[1]Department of Obstetrics and Gynaecology, Command Hospital Eastern Command, Kolkata, West Bengal, India
[2]Department of Obstetrics and Gynaecology, Command Hospital Air Force, Bangalore, Karnataka, India
[3]Department of Obstetrics and Gynaecology, Armed Force Medical College, Pune, Maharshtra, India

*Correspondence:
Dr. Vinod G. Nair,
E-mail: nair.vinod19@gmail.com

ABSTRACT

Background: Diabetes Mellitus in pregnancy has long been recognized as a serious problem for both mother and fetus. Gestational Diabetes Mellitus (GDM) is defined as carbohydrate intolerance of variable severity with onset or first recognition during pregnancy. Even though there are many diagnostic criteria and guidelines for management of GDM, there still exists lack of consensus regarding diagnosis and management of patients with GDM. After Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, International Association of Diabetes in Pregnancy Study Group (IADPSG) has formulated a new consensus guideline for diagnosing hyperglycaemia in pregnancy which has formed the back bone for this particular study. The aim of this study was to assess the incidence of GDM using current international consensus guidelines with 75g Oral Glucose Tolerance Test (OGTT) and evaluation of maternal and fetal outcome.
Methods: All antenatal patients were screened for GDM with 75g OGTT and their glycaemic control was evaluated throughout pregnancy. Either Medical Nutritional Therapy or Oral Hypoglycaemic Agents or Insulin Therapy was advised for glycaemic control. Maternal and neonatal outcomes were evaluated.
Results: A total of 856 Antenatal patients were screened and 111 were diagnosed as GDM, showing an incidence of 13%. Medical Nutritional Therapy was found to be an effective method for glycaemic control in GDM.
Conclusions: The incidence of GDM in the studied population was found to be 13%. Previous history of GDM was found to be the most significant high risk factor associated with GDM followed by family history of Diabetes. Medical Nutritional Therapy was found to be highly effective in the management of GDM. Only 9% of GDM patients required insulin therapy. With adequate glycaemic control, all late pregnancy complications and neonatal complications can be alleviated.

Keywords: Gestational diabetes mellitus, Oral glucose tolerance test, Perinatal outcome

INTRODUCTION

Gestational Diabetes Mellitus (GDM), a common medical complication of pregnancy, is defined as "any degree of glucose intolerance with onset or first recognition during pregnancy".[1,2] The initial criteria for its diagnosis were established more than 40 years ago and, with modifications, remain in use today.[3,4] These criteria were chosen to identify women at high risk for development of diabetes after pregnancy or were derived from criteria used for nonpregnant individuals and not necessarily to identify pregnancies with increased risk for adverse perinatal outcome.[5,6]

There is consensus that overt diabetes during pregnancy is associated with significant risk of adverse perinatal outcome. The risk of adverse perinatal outcome associated with degrees of hyperglycemia less severe than overt diabetes is controversial. Several factors contribute to this longstanding controversy. Some have attributed risks of adverse outcomes associated with GDM, such as birth weight that is large for gestational age (LGA), excess fetal adiposity, and higher rate of cesarean section, to confounding characteristics, such as obesity, more advanced maternal age, or other medical complications, rather than glucose intolerance.[7-9] Bias of caregivers toward expectation of adverse outcomes may increase morbidity due to increased intervention.[10] Some suggest that criteria currently in wide use for the diagnosis of GDM are too restrictive and that lesser degrees of hyperglycemia increase risk of adverse perinatal outcomes.[11-16] Conversely, others believe that systematic efforts to identify GDM should be stopped unless data become available to link significant morbidities to specific degrees of glucose intolerance.[8] Lack of international uniformity in the approach to ascertainment and diagnosis of GDM has been a major hurdle.[2]

The Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study was designed to clarify risks of adverse outcome associated with degrees of maternal glucose intolerance less severe than those with overt diabetes during pregnancy.[17] HAPO study results were considered in depth in arriving at the recommendations for diagnosis of GDM.[18,19] The objective of the HAPO study was to clarify associations of levels of maternal glucose lower than those diagnostic of diabetes with perinatal outcome.[17,18] This was accomplished by performing a 75-g oral glucose tolerance test (OGTT) on a heterogeneous, multinational, multicultural, ethnically diverse cohort of ~25,000 women in the third trimester of gestation. Primary outcomes in the blinded HAPO cohort were birth weight >90th percentile, primary cesarean section delivery, clinically defined neonatal hypoglycemia, and cord C-peptide >90th percentile. Secondary outcomes were preeclampsia, preterm delivery, shoulder dystocia/birth injury, hyperbilirubinaemia, and intensive neonatal care. Importantly, there were continuous graded relationships between higher maternal glucose and increasing frequency of the primary outcomes, independent of other risk factors.[18] Similar associations were also observed for secondary outcomes.[18,19] Because associations were continuous with no obvious thresholds at which risks increased, it was concluded that a consensus was required to translate these results into clinical practice. As a result of the extensive efforts used to standardize procedures for participant enrollment, laboratory analyses, data collection, and analysis of results, HAPO data were used as the basis for the new GDM diagnostic thresholds recommended in this report.[17-19] The stepwise consideration of the HAPO study data described above led to the recommendation of the values for FPG, 1-h, and 2-h plasma glucose

concentration indicated in Table 1 as diagnostic thresholds. At least one of these thresholds must be equaled or exceeded to make a diagnosis of GDM.

Table 1: Threshold values for diagnosis of GDM.

Glucose measure	Glucose concentration threshold*		Above threshold (%)
	mg/dl	mmol/l	
FPG	92	5.1	8.3
1-h Plasma glucose	180	10.0	14.0
2-h Plasma glucose	153	8.5	16.1

*One or more of these values from a 75-g OGTT must be equalled or exceeded for the diagnosis of GDM.

Table 2: Threshold values for diagnosis of overt (preconceptional) diabetes in pregnancy.

Measure of glycaemia	Threshold*
Fasting plasma glucose	126 mg/dl
HbA1C	6.5%
Random plasma glucose#	200 mg/dl

*One of these must be met or exceeded to identify the patient as having overt diabetes in pregnancy.
#If a random plasma glucose is the initial measure, the tentative diagnosis of overt diabetes in pregnancy should be confirmed by FPG or A1C using a DCCT/UKPDS-standardized assay.

METHODS

A prospective observational study was carried out for one year at a tertiary care centre on 856 antenatal cases to determine incidence and outcome of GDM using 75g OGTT. All antenatal patients were screened for GDM except those who had pre-existing Diabetes. As per the institutional policy, every patient was advised 75g OGTT at her first antenatal visit. However, the test was deferred till the nausea and vomiting of early pregnancy subsided. In such patients, Fasting and Post Prandial plasma glucose were asked for. But, all such patients including those who had a normal OGTT result in the first visit definitely underwent a 75g OGTT between 24-28 wks period of gestation.

All patients who were diagnosed to have GDM were advised to take Medical nutritional therapy (MNT). The total per day Calorie requirement was calculated for each patient of GDM according to her pre-pregnancy BMI and present body weight. Daily calorie requirement for an average Indian woman is approximately 1600 kcal/day and she requires about 1700, 1800 and 1900kcal/day in 1st, 2nd and 3rd trimester of pregnancy respectively. Patients' ethnicity, food preferences etc. were considered while formulating a diet plan for them. Food items with high glycaemic index were avoided. Patients were encouraged to consume citrus fruits.

The total calories per day were divided into three meals; breakfast, lunch and dinner. Each of these meals was further subdivided into a major meal and a minor meal. Each major meal constituted 2/3rd and each minor meal 1/3rd of the food items planned to be consumed during that part of the day. The time gap between a major meal and a minor meal was fixed as 3hrs. Every patient maintained a 'Diet Diary' in which she recorded her daily divided dietary intake. Total calories consumed were calculated every day and dietary modification, if any, was advised to the patient.

After three days of Medical nutritional therapy (MNT), all patients underwent six point plasma glucose profiles which included fasting, post prandial, before lunch, after lunch, before dinner and after dinner plasma glucose measurement. All post meal samples were collected after 2hrs of major meal.

The above plasma glucose profile was critically analyzed. The target glucose level for each pre-meal sample was taken as 95 mg/dl and those for post meal samples were taken as 140 mg/dl. Patients were advised dietary modification and / or exercise for minor deviations of one or two values in the profile. However, three or more abnormal values were considered as an indicator of failed medical nutritional therapy and alternative regimes for glycaemic control were opted for in such patients.

Patients with deranged plasma glucose profile with three or more abnormal values with no pre-meal value exceeding 105mg/dl were considered for therapy with oral hypoglycaemic agents. The drug used was Tab Glibenclamide in a dosage starting from 2.5mg twice daily to a maximum of 20mg/day. However, there was no patient who met the criteria for initiating Glibenclamide in the study.

Patients with deranged plasma glucose profile who didn't meet criteria for oral hypoglycaemic Therapy were treated with insulin human mixtard (30:70). Total requirement of Insulin per day for a Gravida, is approximately 0.7, 0.8 and 0.9 units /kg body wt in 1st, 2nd and 3rd trimester respectively. Only 2/3rd of the above calculated dose was administered, of which 2/3rd was administered in the morning and 1/3rd in the evening.

After at least three days on Insulin, all patients on Insulin Therapy underwent a Seven Point Plasma Glucose Profile, which included a 2 am value. Dose adjustments and titration of Insulin dosage was done as per the laid down criteria. All patients were monitored with 3-4 weekly plasma glucose profile. All pregnancies were terminated at or before 39 completed weeks period of gestation.

Glycosylated Hemoglobin (HbA1C) was measured in every patient who was detected to have GDM in the first trimester. Patients with an HbA1C value ≥7.5 % were offered MTP.

All parturients with GDM were monitored as per guidelines for Labour Monitoring in high risk pregnancy. A strict Glycaemic control was followed and Plain Insulin was administered as per sliding scale with a 2 hourly capillary glucose monitoring as described in Table 3.

Table 3: Sliding scale of insulin for parturients.

Capillary glucose (mg/dl)	Insulin requirement
≤100	No Insulin. Glucose containing IV fluids (5% Dextrose / Dextrose Normal saline)
100-140	Plain Insulin 1Unit/hr along with Glucose containing IV fluids.
140-200	Plain Insulin 2 Units/hr with Crystalloids
200-240	Plain Insulin 4 Units/hr with Crystalloids
240-280	Plain Insulin 6 Units/hr with Crystalloids

Cord blood was collected for plasma Glucose measurement in every case. All neonates of GDM mothers were closely observed for development of Respiratory Distress, Hypoglycaemia or Seizures during first 24 hrs of birth. Capillary glucose was measured every 3 hourly. A Glucose level less than 40 mg/dl was considered as Hypoglycaemia. Every neonate was observed for appearance of jaundice and phototherapy was implemented as per advice of Paediatric team.

RESULTS

Incidence of GDM

Out of 856 antenatal patients screened, 111 were diagnosed as GDM. The incidence of GDM was calculated as 13% (Table 4).

Table 4: Incidence of GDM as per age distribution of cases.

Age group	Total cases	% of total population	No of GDM cases	Incidence of GDM
<20 yrs	23	2.68	2	8.69
20-25 yrs	373	43.55	39	10.45
26-30 yrs	347	40.54	56	16.13
31-35 yrs	100	11.67	13	13
>35 yrs	13	1.51	1	7.69
Total	856	100	111	13

As depicted in Table 4 above, it can be concluded that GDM is most commonly detected in the age group of 26 to 30yrs.

Association with high risk factors

Figure 1 depicts the incidence of GDM in high risk group in comparison with low risk antenatal population. From the graph it can be concluded that previous history of GDM is a 100% predictor of GDM in the current pregnancy. After previous history of GDM, it is the family history of Diabetes in first degree relatives which has shown close association with development of GDM.
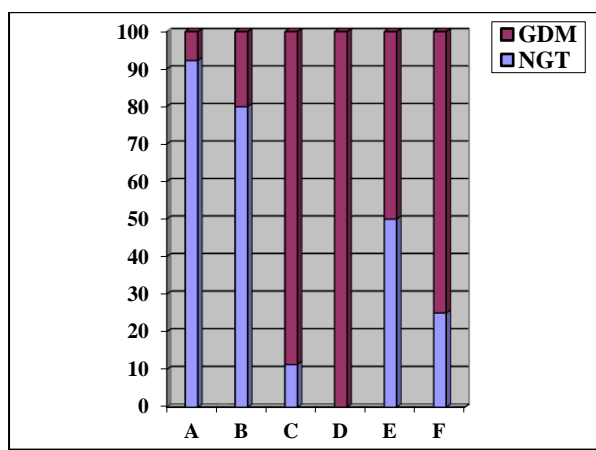

A = Age ≥35yrs
B=Pre-pregnancy BMI ≥30 kg/m^2
C = Family h/o Diabetes
D = Previous h/o GDM
E = Previous h/o Macrosomia
F = Previous h/o IUFD

Figure 1: incidence of GDM in high risk group.

Obstetric outcome

Obstetric outcome in each GDM patient was analyzed and was compared with that of other patients. In our study, it was found that almost all adverse obstetric outcomes due to GDM were decreased to a level comparable with that of other patients (Figure 2).
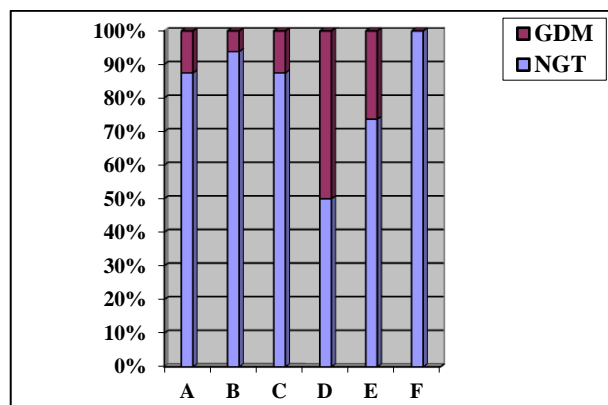
A = Total deliveries
B = LSCS for Dystocia
C = Instrumental del. for dystocia
D = MTP for Cong. Anomalies
E = Early pregnancy failure
F = Unexplained IUFD

Figure 2: comparison of obstetric outcome between GDM and normal glucose tolerance (NGT) group.

Neonatal outcome

There were a total of 828 neonates born during the study period of one year, out of which 105 were born to GDM mothers. There was no neonate with macrosomia born during the study period. Birth weight of ≥4.0 kg was taken as the cut off for defining macrosomia (Table 5).

Table 5: Neonatal outcome.

	Total neonates	Macrosomia	Term neonates with RDS	Hypoglycaemia	Hyperbilirubinaemia
Total Neonates	828	0	41	5	141
Born to GDM	105	0	4	0	4
Percentage	12.68	0	8.33	0	2.83
Born to NGT	723	0	37	5	137
Percentage	87.32	0	91.67	100	97.17

DISCUSSION

In our study, the incidence of gestational diabetes was found to be 13%. The method used for diagnosing GDM was the new international consensus guideline as recommended by IADPSG. As evident from other studies, it was found that there is no substantial difference in the frequency of GDM compared to other criteria for diagnosis of GDM. GDM prevalence has been reported variably from 1.4 to 14% worldwide and differently among racial and ethnic groups. Many studies have been conducted in Indian population as well and an overall incidence of 5-15% has been reported. Wendland et al. compared the IADPSG and WHO criteria using 75g OGTT.[20-25] They concluded that both the criteria identified women at a small increased risk for adverse pregnancy outcome. Associations were of similar

magnitude for both criteria. However, high inconsistency was found for those with IADPSG criteria. In another Californian study conducted by Sach et al. to find out the frequency of GDM at collaborating centres based on IADPSG consensus panel recommended criteria, an overall GDM frequency of 17.8 % (range 9.3-25.5 %) was reported.[26] It was also found that there is a substantial centre-to-centre variation in which glucose measures met diagnostic thresholds. They concluded that although the new diagnostic criterion for GDM applies globally, centre-to-centre differences occur in GDM frequencies and relative diagnostic importance of Fasting, 1hour and 2hour glucose levels. This may impact global strategies for diagnosis of GDM. In a study conducted at Dr. V Seshiah Diabetic Research Institute and Dr. Balaji Diabetes Care Centre Chennai, India, Diabetes in Pregancy Study group in India (DIPSI) criteria was used for diagnosis of GDM.[27] In that, they found an incidence of 13.4 %. Also it was found that, 9.7 % of GDM population required Insulin therapy.

In our study, a 90 % association was found between high risk and development of GDM. Also, it was found that previous history of GDM is a 100 % predictor of development of GDM in subsequent pregnancies. Family history of GDM was found to be the next most common predictor for GDM. In a study conducted in Portugal by Detch JC et al, for determining the markers for diagnosis of GDM, it was found that risk factor was associated with 95 % of the GDM population.[28] The most relevant risk factor was found to be previous history of GDM. Risk factors were found to be very sensitive in GDM detection and provision of family history of Diabetes Mellitus strengthens its relationship with Type 2 Diabetes.

In our study, it was found that all the late pregnancy and perinatal complications like macrosomia, IUFD, birth injuries, dystocia etc. were alleviated by maintaining an adequate glycaemic control in the antenatal period. Kwik et al. in their study compared the obstetric outcome in treated and untreated GDM.[29] They found that obstetric outcome is affected by glucose intolerance. In the untreated GDM group, there were more macrosomia, more number of caesarian sections or instrumental deliveries for dystocia and birth injuries. In the treated group, the outcome was comparable to euglycaemic population. In another study conducted by Most OL et al, they found that adverse perinatal outcome is significantly higher in those women who were diagnosed to have GDM in the early pregnancy.[30] The adverse pregnancy outcome was unaffected despite early identification and management of GDM implying greater severity of the disease.

In our study, it was found that neonatal complications associated with GDM like macrosomia, hypoglycaemia, hyperbilirubinaemia and RDS were reduced to a level comparable to those of euglycaemic group. In fact, there were 5 neonates who had hypoglycaemia in the NGT group and none in GDM group. None of the neonates was macrosomic. RDS requiring NICU admission was studied as a neonatal outcome and it was found that comparatively lesser number of neonates of GDM mothers suffered from RDS. It was concluded that good glycaemic control in the antenatal period in GDM prevents macrosomia and other neonatal complications. A retrospective study conducted by Mitanchez et al. to evaluate risk of perinatal complications in infants born to mothers with GDM proved that untreated moderate or severe GDM increases the risk of fetal and neonatal complications.[31] The risk of malformations slightly increases in newborns of mothers with GDM compared to the general population. The risk is probably associated with the presence of undiagnosed Type 2 diabetes Mellitus. Also the study concluded that there is linear relationship between maternal blood glucose level and increased birth weight. Treatment of GDM reduces macrosomia. The risk of neonatal asphyxia and perinatal mortality are no higher in infants born to women with GDM. Birth injuries are more likely to occur in cases of untreated GDM. Incidence of hypoglycaemia and hyperbilirubinaemia were found to be similar to general population. Macrosomia has been demonstrated to be the predominant adverse outcome in case of GDM.[31] There is a linear relationship between maternal blood glucose level and increased birth weight. Treatment of GDM reduces macrosomia and thus prevents adverse neonatal outcome.

REFERENCES

1. American Diabetes Association Diagnosis and classification of diabetes mellitus (Position Statement). Diabetes Care. 2009;32(1):S62-7.
2. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus: the organizing committee. Diabetes Care. 1998;21(2):B161-7.
3. O'sullivan JB, Mahan CM. Criteria for oral glucose tolerance test in pregnancy. Diabetes. 1964;13:278-85.
4. Cutchie WA, Cheung NW, Simmons D. Comparison of international and New Zealand guidelines for the care of pregnant women with diabetes. Diabet Med. 2006;23:460-8.
5. Metzger BE, Buchanan TA, Coustan DR, De Leiva A, Dunger DB, Hadden DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care. 2007;30(2):S251-60.
6. World Health Organization: WHO Expert Committee on Diabetes Mellitus: Second Report Geneva, World Health Org., 1980. (Tech. Rep. Ser., no. 646).

7. Jarrett RJ. Reflections on gestational diabetes. Lancet. 1981;28:1220-1.
8. Hunter DJS, Keirse MJNC. Gestational diabetes in effective care. In Pregnancy and Childbirth Chalmers I, Enkin M, Kierse M, editors. Eds. New York, Oxford University Press; 1989:403-410.
9. Spellacy WN, Miller S, Winegar A, Peterson PQ. Macrosomia: maternal characteristics and infant complications. Obstet Gynecol. 1985;66:158-61.
10. Coustan DR. Management of gestational diabetes: a self-fulfilling prophecy? JAMA. 1996;275:1199-200.
11. Jensen DM, Damm P, Sørensen B, Mølsted-Pedersen L, Westergaard JG, Klebe J, et al. Clinical impact of mild carbohydrate intolerance in pregnancy: a study of 2904 nondiabetic Danish women with risk factors for gestational diabetes. Am J Obstet Gynecol. 2001;185:413-9.
12. Yang X, Hsu-Hage B, Zhang H, Zhang C, Zhang Y, Zhang C. Women with impaired glucose tolerance during pregnancy have significantly poor pregnancy outcomes. Diabetes Care. 2002;25:1619-24.
13. Vambergue A, Nuttens MC, Verier-Mine O, Dognin C, Cappoen JP, Fontaine P. Is mild gestational hyperglycaemia associated with maternal and neonatal complications? the Diagest Study. Diabet Med. 2000;17:203-8.
14. Langer O, Brustman L, Anyaegbunam A, Mazze R. The significance of one abnormal glucose tolerance test value on adverse outcome in pregnancy. Am J Obstet Gynecol. 1987;157:758-63.
15. Sacks DA, Abu-Fadil S, Greenspoon JS, Fotheringham N. Do the current standards for glucose tolerance testing in pregnancy represent a valid conversion of O'Sullivan's original criteria? Am J Obstet Gynecol. 1989;161:638-41.
16. Ferrara A, Weiss NS, Hedderson MM, Quesenberry CP, Selby JV, Ergas IJ, et al. Pregnancy plasma glucose levels exceeding the American Diabetes Association thresholds, but below the National Diabetes Data Group thresholds for gestational diabetes mellitus, are related to the risk of neonatal macrosomia, hypoglycaemia and hyperbilirubinaemia. Diabetologia. 2007;50:298-306.
17. HAPO Study Cooperative Research Group The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. Intl J Gynaecol Obstet. 2002;78:69-77.
18. HAPO Study Cooperative Research Group. Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, et al. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study Cooperative Research Group Hyperglycemia and adverse pregnancy outcomes. N Engl J Med. 2008;358:1991-2002.
19. HAPO study cooperative research group hyperglycemia and adverse pregnancy outcome (HAPO) study: associations with neonatal anthropometrics. Diabetes. 2009;58:453-9.
20. Seshiah V, Balaji V, Balaji MS, Paneerselvam A, Arthi T, Thamizharasi M, et al. Prevalence of gestational diabetes mellitus in South India (Tamil Nadu) - a community based study. J Assoc Physicians India. 2008;56:329-33.
21. Seshiah V, Sahay BK, Das AK, Shah S, Banerjee S, Rao PV, et al. Gestational Diabetes Mellitus - Indian Guidelines. J Indian Med Assoc. 2009;107:799-802, 804-6.
22. Wahi P, Dogra V, Jandial K, Bhagat R, Gupta R, Gupta S, et al. Prevalence of gestational diabetes mellitus (GDM) and its outcomes in Jammu region. J Assoc Physicians India. 2011;59:227-30.
23. Das V, Kamra S, Mishra A. Screening for gestational diabetes and maternal and fetal outcome. J Obstet Gynaecol India. 2004;54:449-51.
24. Bhattacharya C, Awasthi RT, Kumar S, Lamba PS. Routine screening for gestational diabetes mellitus with glucose challenge test in antenatal patients. J Obstet Gynaecol India. 2001;51-75.
25. Wenderland EM, Torloni MR, Falavigna M et al. Gestational Diabetes Mellitus and pregnancy outcome: A systematic review of the WHO and IADPSG diagnostic criteria. J BMC pregnancy and childbirth. 2012;12-23.
26. Sach DA, Hadden CR, Maresh M. Frequency of GDM at collaborating centres based on IADPSG consensus panel recommended criteria: the HAPO study. J Diabetes Care. 2012;35(3);526-8.
27. Balaji V, Balaji M, Anjalakshi C. Diagnosis of GDM in Asian – Indian mothers. J India J Endocrinol Metab. 2011;15(31):187-90.
28. Detch JC, Almeida AC, Bortolini LG. Markers for diagnosis and treatment in 924 pregnancies with GDM. J Arq Bras Endocrinol Metabol. 2011;55(6)389-98.
29. Kwik M, Secho SK, Smith C. Outcome of pregnancies affected by Impaired Glucose Tolerance. J Diabetes Res Clin Pract. 2007;77(2):263-8.
30. Most OL, Kim JH, Hrslem AA. Maternal and neonatal outcome in early glucose tolerance testing in an obstetric population in New York. J Perinat Med. 2009;37(2):114-7.
31. Mitanchez D. Fetal and neonatal complications in GDM; perinatal mortality, congenital malformations, macrosomia, shoulder dystocia, birth injuries, neonatal complications. J Diabetes Metab. 2010;36(6.2):617-27.