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ORIGINAL RESEARCH

A Hospital Based Prospective Study to Determine the Incidence of Insulin Resistance and Gestational Diabetes Mellitus in the Antenatal Population and for Their Maternal and Foetal Outcomes

[1]Pradeep Kumar Chouhan, [2]Usha Rangey Chouhan

[1]Principal Specialist, Department of Medicine, Government District Hospital, Sirohi, Rajasthan, India
[2]Senior Specialist, Department of Obst. & Gynae., Government District Hospital, Sirohi, Rajasthan, India

Correspondence:
Usha Rangey Chouhan
Senior Specialist, Department of Obst. & Gynae., Government District Hospital, Sirohi, Rajasthan, India.
Email: drushapradeepchouhanms@gmail.Com

ABSTRACT

Background: Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance occurringfor the first time during pregnancy. The prevalence of GDM varies in direct proportion to theprevalence of Type 2 diabetes for a given ethnic group or population. It is crucial to detectwomen with GDM as the condition is associated with diverse range of adverse maternal andneonatal outcomes. This study aims at determining the incidence of insulin resistance and gestational diabetes mellitus in the antenatal population and for their maternal and foetal outcomes.

Materials& Methods: A hospital based observational prospective study done on all pregnant women attending the antenatal clinic in government district hospital, Sirohi, Rajasthan, India during one year period.Screening for Insulin Resistance was done at the time of booking or the first antenatalvisit if they met the criteria for the high risk group, by Fasting Serum Insulin and FastingPlasma Glucose levels.IR value calculated with HOMA-2IR software and value > 1.8 wastaken as cut off for insulin resistance. Patients labelled GDM were started on specifictreatment with medical nutrition therapy, oral hypoglycaemic agent and insulin therapy. Theywere then followed up till term ensuring adequate glycaemic control with 3 weeklysupervised hospitalized blood sugar profile. Maternal and foetal outcomes were there afterdocumented and studied.

Results:Our study showed that total no. of antenatal patients was 500 during one year study period and 55 (11%) patients detected insulin resistance and gestational diabetes mellitus. So, the incidence of carbohydrate intolerance was 11%.The mean age of these pregnant women was 28.56±4.23 years.Our results shows that positive statistically significant correlationbetween insulin resistance and development of glucose intolerance (p <0.0001). The present study shows that there is no statistical significant association between development of Gestational Hypertension and Insulin Resistance (P>0.05).

Conclusion: We concluded that early detection and institution of specific treatment of glucose intolerance with MNT/ OHA/ Insulin therapy certainly gives better maternal and neonatal outcomes.The costeffectiveness and simplicity of this model of care makes it suitable for countries with highprevalence of glucose intolerance.

Keywords: Insulin resistant, Gestational diabetes, HOMA-2IR, Diabetes mellitus

INTRODUCTION

Physiological changes in pregnancy include a state of insulin resistance which as aprotective measure ensures glucose availability for the growing foetus at the cost of mother'scatabolic status. Over the course of pregnancy, fasting glucose levels decrease as hepaticglucose levels increase. In the normal case, the hepatic glucose production is restrained byinsulin. The hepatic glucose production increases despite increasing fasting insulinconcentrations, resulting in a decrease in maternal hepatic insulin sensitivity leading to adecreased suppression of hepatic glucose production.

Insulin resistance (IR) in fat cells reduces the effects of insulin and results in increasedhydrolysis of stored triglycerides. Increased mobilization of stored lipids in these cellselevates free fatty acids in the blood plasma. Insulin resistance in muscle cells reducesglucose uptake and so local storage of glucose as glycogen is reduced. IR in liver cellsresults in impaired glycogen synthesis and a failure to suppress glucose production.

Women diagnosed with GDM have higher fasting glucose concentrations; however,the basic hepatic glucose production does not differ from women with normal glucosetolerance. In the case of GDM, there is an imbalance between tissue insulin requirements forregulation of glucose and the ability of the β-cells in the pancreas to meet the requirements.

Gestational diabetes mellitus (GDM), a common medical complication of pregnancy,is defined as "any degree of glucose intolerance with onset or first recognition duringpregnancy".[1,2] GDM has been studied extensively for more than 40 years, but there is still alack of a good foundation of scientific data on which to make evidence-based decisionsregarding treatment. In clinical practice, data from women with pregestational diabetes havebeen extrapolated to women with GDM.

Some studies have also convincingly indicated that there is an association betweenglucose intolerance and maternal as well as perinatal complications, in particular foetalmacrosomia and resultant shoulder dystocia, and caesarean delivery.[3,4] Very few prospective studies on GDMhave been carried out, and virtually no randomized controlled data for subjects in whomGDM is left untreated are available.

Some have attributed risks of adverse outcomes associated with GDM, such as birthweight that is large for gestational age (LGA), excess foetal adiposity, and higher rate ofcaesarean section, to confounding characteristics, such as obesity, more advanced maternalage, or other medical complications, rather than glucose intolerance[5-7]. Bias of caregiverstoward expectation of adverse outcomes may increase morbidity due to increasedintervention[8]. Some suggest that criteria currently in wide use for the diagnosis of GDM aretoo restrictive and that lesser degrees of hyperglycaemia increase risk of adverse perinataloutcomes[9-12]. Conversely, others believe that systematic efforts to identify GDM should bestopped unless data become available to link significant morbidities to specific degrees ofglucose intolerance[6]. Lack of international uniformity in the approach to ascertainment anddiagnosis of GDM has been a major hurdle[2].

Importantly, there were continuous graded relationships between higher maternalglucose and increasing frequency of the primary outcomes, independent of other risk factors. Similar associations were also observed for secondary outcomes.[13,14] Associations did notdiffer among centres; thus, the results were applicable to all centres and could be usedglobally to develop outcome-based criteria for classifying glucose metabolism in pregnancy.Because associations were continuous with no obvious thresholds at which risks increased, itwas concluded that a consensus was required to translate these results into clinical practice.This study aims at determining the incidence of insulin resistance and gestational diabetes mellitus in the antenatal population and for their maternal and foetal outcomes.

MATERIAL & METHODS

A hospital based observational prospective study done on all pregnant women attending the antenatal clinic in government district hospital, Sirohi, Rajasthan, India during one year period.

INCLUSION CRITERIA

- Pregnant women with diagnosed Gestational Diabetes Mellitus.
- Clinical markers of insulin resistance :-

a) BMI > 30 kg/m2
b) History of macrosomia in previous pregnancies
c) Acanthosis nigricans or skin tags
d) History of Poly cystic ovarian syndrome or Oligomenorrhoeic cycles.
e) Family history of Diabetes Mellitus (first-degree relatives).
f) Acne.

- Abnormal HOMA-2IR value (> 1.8)

EXCLUSION CRITERIA

- Pregnant women already on treatment with insulin sensitizers / oral hypoglycaemicagents.
- Women with Pre-gestational diabetes mellitus.
- Women with pre-existing medical disorders other than anemia.

METHODS

To determine if gestational diabetes is present in pregnant women, a standard OGTTwas performed after overnight fasting (8-14 hours) by giving 75g of anhydrous glucose in250-300 ml of water. Plasma glucose was measured fasting, after 1 hour and after 2 hours.

Pregnant women who met the revised IADPSG criteria for diabetes mellitus were classified as GDM and others who had normal OGTT result were classified as Normal GlucoseTolerant (NGT).

INSULIN RESISTANCE

HOMA-2IR value of more than 1.8 has been taken as cut-off for the measure ofinsulin resistance. Screening for insulin resistance was done at the time of booking by serumfasting insulin and fasting plasma glucose levels.

All antenatal patients were screened for GDM except those who had pre-existingdiabetes. As per institutional policy, every patient was advised 75gm OGTT at her firstantenatal visit. However, the test was deferred till the nausea and vomiting of earlypregnancy subsided. In such patients, Fasting and Post-prandial plasma glucose were askedfor. But, all such patients including those who had normal OGTT result in the first antenatalvisit were subjected to 75g OGTT between 24-28 weeks Period of Gestation.

Screening for Insulin Resistance was done at the time of booking or the first antenatalvisit if they met the criteria for the high risk group, by Fasting Serum Insulin and FastingPlasma Glucose levels.

HIGH RISK GROUP

a) Pre-pregnancy BMI > 30kg/m2
b) History of DM in the family (first degree relative).
c) History of GDM in previous pregnancy
d) History of macrosomia in previous pregnancy
e) Acanthosis nigricans or skin tags.

f) History of PCOS or oligomenorrhoeic cycles.
g) Acne
h) Age ≥ 35 years

HOMA calculator (software based) was used to calculate the HOMA-2IR value whichwas taken as the measure for Insulin Resistance.

All patients were followed up through their antenatal and post natal course and salient outcome measures pertaining to the Obstetric and Neonatal outcomes were recorded anddocumented.

RESULTS

Our study showed that total no. of antenatal patients was 500 during one year study period and 55 (11%) patients detected insulin resistance and gestational diabetes mellitus. So, the incidence of carbohydrate intolerance was 11%.

Insulin resistance in patients studied, was defined as patients having HOMA-2IR value more than 1.8. Out of 55 patients, 13 patients had insulin resistance in our study. Our results shows that positive statistically significant correlation between insulin resistance and development of glucose intolerance (p <0.0001).

Table 1: Analysis Between Insulin Resistance Vs Glucose Intolerance

Insulin Resistance	Glucose Intolerance		Total	P-value
	Yes	No		
Yes	13	0	13	<0.001*
No	42	445	487	
Total	55	445	500	

The present study shows that there is no statistical significant association between development of Gestational Hypertension and Insulin Resistance (P>0.05) (table 2).

Table 2: Analysis Between Gestational hypertension vs average HOMA-2IR

Insulin Resistance	Gestational hypertension		Total	P-value
	Yes	No		
Yes	2	11	13	>0.05
No	4	38	42	
Total	6	49	55	

Our study shows that maximum number of vaginal and caesarean sections happened with patients with BMI between 25 to 29.9 kg/m2 group (table 3).

Table 3: BMI Vs MODES OF DELIVERY

BMI (kg/m2)	Vaginal delivery	LSCS	Total	Average HOMA 2IR
20.0-24.99 kg/m2	11	3	14	0.845
25.0-29.99 kg/m2	25	13	38	1.53
30.0-34.9 kg/m2	3	0	3	2.734
Total	39	16	55	

No cases of Macrosomia, indirectly indicates the success of the therapeutic institutional protocol to which the patients of the study group were subjected to during antenatal period (table 4).

Table 4: Comparative Analysis Of Newborn Birth Weight And Mode Of Therapy Instituted For Carbohydrate Intolerance

Birth weight (kg)	MNT	MNT+OHA	MNT+IT
<3 kg	14	10	5

>3 kg	22	2	2
Total	36	12	7

DISCUSSION

This study is an attempt to establish the causal relationship between the need for anestablished screening guideline for development of carbohydrate intolerance in women andfurther their respective obstetrical outcomes (maternal and neonatal). The population under study was adequately randomized in view of women hailingfrom different ethnic and culturally diverse segments of society in India formingrepresentative groups from different parts of the country.

Gestational diabetesensues when the woman's insulin secretary capacity is inadequate to overcome theprogressive insulin resistance. It is often associated with maternal risk factors, such asoverweight, advanced age and a previous complicated obstetric history.[15,16] It has been claimedthat the higher rate of complications can be ascribed to these risk factors and not to the hyperglycaemic condition itself.[6]

In our study, the incidence of carbohydrate intolerance was found to be 11%.The criteria used in our study were the new international consensus guideline asrecommended by IADPSG. As evident from other studies, it was found that there is nosubstantial difference in the frequency of GDM compared to other screening methods forGDM. Also it was noted that majority of the studied cases had only elevated FPG in OGTT.

This group accounted for 85.6 % of the population studied.GDM prevalence has been reported variably from 1.4% to 14 % worldwide anddifferently among racial and ethnic groups. Many studies have been conducted in Indianpopulation as well[17,18] and an overall incidence of 5-15% has been reported.

Wendland et al.[19] compared the IADPSG and WHO criteria using 75g OGTT.Theyconcluded that both the criteria identified women at a small increased risk for adversepregnancy outcome. Associations were of similar magnitude for both criteria however, highconsistency was found for those with IADPSG criteria.

In a Californian study, Sach et al.[20] found the frequency of GDM at different collaboratingcentres based on IADPSG consensus panel recommended criteria, an overall GDMfrequency of 17.8%. Though there was substantial centre to centre variation in which glucosemeasures met diagnostic thresholds. They concluded that although the new diagnosticcriteria for GDM applied globally, centre to centre differences occur which may impactglobal strategies for diagnosis of GDM.

In a study conducted at Dr.Seshiah et al.[21], India, DIPSI (Diabetes in pregnancy studygroup) criteria was used for the diagnosis of GDM. They found an incidence of 13.4% andfurther found that 9.7% of GDM required insulin therapy.

The prevalence of insulin resistance in the total antenatal patients studied in our hospitalduring the period of study was 2.6%.Voldner N et al.[22] in their study reported that women (BMI>25kg/m2) in early pregnancyhad levels of insulin sensitivity that were lower throughout pregnancy as compared to thenormal weight women, this reduction was significant ($p < 0.0001$). Amongst the various screening methods, BMI has a high sensitivity (85%) and a goodnegative predictive value (98%).

Further it can be argued that pregnant ladies with pre-pregnancy BMI > 25kg/m2 shouldbe screened for IR and should be started on medical nutrition therapy as a preventivemeasure.

The results of association between development of gestational hypertension in earlyand mid-trimester in glucose intolerant patients as an outcome measure with insulinresistance showed no statistically significant correlation between the two variables , $p>0.05$. This result is supported by a study conducted by Romero Gutierrez G et al.[23] in 2005where they the insulin resistance assessed in the third trimester of the pregnancy did nothave association with the

pregnancy induced hypertension and they recommended to carryout further investigations with prospective design and assessing insulin resistance calculatingthe homeostasis model assessment during all the pregnancy to evaluate this possible was association.
It is rational to conclude that there is insignificant association between hypertensivedisorders of pregnancy and IR as measured by HOMA-2IR. They may be considered as anindependent entity with different pathogenesis causing adverse pregnancy outcome.

CONCLUSION

We concluded that early detection and institution of specific treatment of glucose intolerance with MNT/ OHA/ Insulin therapy certainly gives better maternal and neonatal outcomes.

REFERENCES

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus (Position Statement). Diabetes Care 2009;32(Suppl. 1):S62–S67
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(Suppl. 2):B161–B167.
3. Langer O, Brustman L, Anyaegbunam A,Mazze R. The significance of one abnormalglucose tolerance test value on adverse outcome in pregnancy. Am J ObstetGynecol987;157:758–763
4. Naylor C.D., Sermer M., Chen E., SykoraK.TorontoTrihospital Gestational DiabetesInvestigators Cesarean delivery in relation to birth weight and gestational glucose tolerance:pathophysiology or practice style? JAMA1996 ; 275 : 1165-1170.
5. Jarrett RJ. Reflections on gestational diabetes.Lancet 1981;28:1220–1221
6. Hunter DJS, Keirse MJNC. Gestational diabetes in effective care. In Pregnancy and Childbirth. Chalmers I, Enkin M, Kierse M, Eds. New York, Oxford University Press, 1989:403–410.
7. Spellacy WN, Miller S, Winegar A, Peterson PQ. Macrosomia: maternal characteristics and infant complications. ObstetGynecol1985;66:158–161.
8. Coustan DR. Management of gestational diabetes: a self-fulfilling prophecy? JAMA 1996;275:1199–1200
9. Jensen DM, Damm P, Sorensen B, Molsted- Pedersen L, Westergaard JG, Klebe J, Beck-Nielsen H. Clinical impact of mild carbohydrate intolerance in pregnancy: a study of 2904 nondiabetic Danish women with risk factors for gestational diabetes. Am J ObstetGynecol, 2001;185:413– 419
10. 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;25:1619–1624
11. 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;17:203–208.
12. 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 ObstetGynecol1989;161:638–641.
13. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, Coustan DR, Hadden DR, McCance DR, Hod M, McIntyre HD, Oats JJ, Persson B, Rogers MS,Sacks DA, Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study Cooperative Research Group. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991–2002.

14. HAPO Study Cooperative Research Group. Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study: associations with neonatal anthropometrics. Diabetes 2009;58:453–459.
15. O'sullivan JB, Mahan CM. Criteria for oral glucose tolerance test in pregnancy. Diabetes 1964;13:278–285.
16. Metzger BE, Buchanan TA, CoustanDR,DeLeiva A, Dunger DB, Hadden DR, Hod M, Kitzmiller JL, Kjos SL, Oats JN, Pettitt DJ, Sacks DA, Zoupas C. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes Care 2007;30(Suppl. 2):S251–S260.
17. Tieu J, Crowther CA, Middleton P. Dietary advice in pregnancy for preventing gestational diabetes mellitus. Cochrane Database Syst Rev. 2008(2):CD006674. 95
18. Moses RG, Barker M, Winter M, Petocz P, Brand-Miller JC. Can a lowglycemic index diet reduce the need for insulin in gestational diabetes mellitus? A randomized trial. Diabetes Care. 2009 Jun;32(6):996-1000.
19. Wendland EM, Torloni MR, Falavigna M, Trujillo J, Dode MA, Campos MA, et al. Gestational diabetes and pregnancy outcomes – A systematic review of the World Health Organization (WHO) and the International Association of Diabetes in Pregnancy Study Groups (IADPSG) diagnostic criteria. BMC Pregnancy Childbirth. 2012;12:23.
20. David A Sacks , David R Hadden, Michael Maresh, ChaicharnDeerochanawong, Alan R Dyer et al. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. Diabetes care 2012 Mar;35(3):526-8.
21. Seshiah V, Balaji V, Balaji MS, Paneerselvam A, Kapur A. Pregnancy and diabetes scenario around the world: India. Int J Gynaecol Obstet. 2009;104:S35–8.
22. Voldner N, Qvisgstad E, Froslie KF, et al. Increased risk of macrosomia among overweight women with high gestational rise in fasting glucose. J Matern Fetal Neonatal Med. 2010;23:74-81.
23. Romero Gutierrez G, Alvarez Cisneros JA, Ponce Ponce de Leon AL. [Association between insulin resistance and pregnancy induced hypertension. Case-control study]. GinecolObstet Mex. 2003 May;71:244-52.