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Impaired glucose tolerance and pregnancy outcome in Chinese women with high body mass index

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To determine if impaired glucose tolerance (IGT) impacts on the outcome of singleton pregnancies in Chinese women with a high (>26 kg/m^2) body mass index (BMI), a retrospective case-control study was performed on 128 women with IGT and 128 controls with normal oral glucose tolerance test results, who were matched for pre-pregnancy BMI (within 0.1 kg/m^2) and delivered within the same 3 year period. The IGT group was older, with more multiparae, a higher incidence of previous gestational diabetes mellitus, higher booking haemoglobin and fasting glucose concentrations, but no difference in the pre-pregnancy weight, gestational weight gain, or weight or BMI at delivery. There was no difference in the obstetric complications, mode of delivery, or the gestational age or mean infant birthweight. However, the birthweight ratio (relative to mean birthweight for gestation), incidence of large-for-gestational-age (birthweight >90th percentile) and macrosomic (birthweight ≥4000 g) infants, and treatment for neonatal jaundice, were significantly higher in the IGT group. The results suggest that some of the complications attributed to gestational diabetes mellitus are probably related to maternal weight excess/obesity in the affected subjects, but IGT could still affect infant birthweight outcome despite diet treatment which has normalized gestational weight gain.

Key words: birthweight/body mass index/impaired glucose tolerance

Introduction

The impact of maternal obesity on pregnancy outcome has been well studied, and increasing obesity is found to be associated with increasing incidence of diabetes mellitus, hypertension, macrosomic and large-for-gestational-age (LGA, birthweight >90th percentile) infants, Caesarean section, and perinatal mortality (Gross *et al*., 1980; Duthie *et al*., 1988; Tilton *et al*., 1989; Naeye, 1990; Johnson *et al*., 1992; Crane *et al*., 1997; Cnattingius *et al*., 1998). There are different recommendations on the classification of weight excess and obesity for the individual. One method is to assess the subject's weight relative to height by the calculation of the body mass index (BMI), which is expressed as the weight in kilograms divided by the square of height measurement in metres. On the basis of the BMI, the subjects can be classified into low BMI (<19.8 kg/m^2), medium BMI (19.8–26 kg/m^2), high BMI (27–29 kg/m^2) and obese (>29 kg/m^2) groups (Institute of Medicine, 1990). Obese women were found to have increased risk of complications such as gestational hypertension and pre-eclampsia, gestational diabetes mellitus (GDM) and Caesarean delivery (Crane *et al*., 1997; Cnattingius *et al*., 1998). However, moderately obese or overweight women were also found to be associated with increased risk of these outcomes as well as fetal death (Tilton *et al*., 1989; Cnattingius *et al*., 1998). Indeed, excessive maternal weight appears to be an important predictor of adverse pregnancy outcome.

On the other hand, maternal weight excess and obesity are associated with increased incidence of GDM (Gross *et al*., 1980; Duthie *et al*., 1988; Tilton *et al*., 1989; Naeye, 1990; Cnattingius *et al*., 1998). As well, women with even mild GDM in the form of impaired glucose tolerance (IGT) by the World Health Organization criteria (WHO, 1980) tended to be heavier with increased BMI (Al-Shawaf *et al*., 1988; Nord *et al*., 1995; Lao and Lee, 1998). In view of the inter-relationship between adverse outcome, maternal obesity, and GDM (Engelgau *et al*., 1995; Galtier-Dereure *et al*., 1995), it is possible that some of the adverse outcomes associated with maternal weight excess were in fact related to the presence of GDM. Conversely, it is also possible that some of the complications attributed to GDM, especially for the milder form of IGT, were actually related to maternal weight excess. This is because it has been reported that good glycaemic control did not normalize birthweight percentiles, but maternal weight at delivery was the only significant predictor of birthweight percentile (Jacobson and Cousins, 1989). Thus IGT diagnosed for the first time in pregnancy might only be a feature of maternal weight excess but not a pathological condition *per se*, as the clinical significance of IGT has also been disputed (Li *et al*., 1987; Nasrat *et al*., 1994).

In our hospital, the incidence of GDM, mostly in the milder form of IGT, has been on the increase over the last decade. It is not clear whether such a phenomenon was merely a reflection of the increasing obesity among women of reproductive age in our society because of the improvement in socio-economic status. There is no data on the effect of maternal IGT on the pregnancy outcome in Asian women with a high BMI. In order to address this question, a retrospective case-control study was performed on subjects with a pre-pregnant BMI > 26 kg/m^2, who were delivered in our hospital over a 3 year period, to determine whether the presence of IGT impacts on the pregnancy outcome.

Materials and methods

Our hospital is a referral centre serving a population that is predominantly (95%) ethnic Chinese. A programme to screen for GDM has been implemented for more than a decade. At the time of the first antenatal visit, women identified as having risk factors for the development of GDM, such as advanced maternal age (>35 years), relevant past obstetric and family history, obesity, and recurrent/significant glycosuria, undergo the 75 g oral glucose tolerance test (OGTT). The result of the OGTT is interpreted by the World Health Organization criteria (WHO, 1980). In addition, all low risk women have random blood glucose testing at the beginning of the third trimester (28–30 weeks) to screen for glucose intolerance. Those with abnormal spot glucose (>5.8 mmol/l if <2 h post-prandial and >5.0 mmol/l if >2 h post-prandial) also undergo the 75 g OGTT.

Women diagnosed with IGT (OGTT 2 h value ⩾8.0 mmol/l) or diabetes mellitus (2 h value ⩾11.0 mmol/l) are categorized as having GDM, as recommended recently (Alberti and Zimmet, 1998). They are referred to a dietitian and put on diet control (30 kcal/kg), and then assessed with pre- and 2 h post-prandial blood sugar profile. Insulin therapy will be started for inadequate control (fasting plasma glucose >5.9 mmol/l and/or post-prandial glucose >7 mmol/l) if dietary readjustment fails to normalize the blood sugar profile. The details of the antenatal management of these mothers have been described before (Lao and Lee, 1998). All the patients who had the OGTT arranged at the clinic are registered.

In this study, firstly the serial numbers and names of the women who underwent the OGTT over a 3 year period, who were carrying singleton pregnancies, and who were delivered in our hospital, were obtained from the registry. During this period, a total of 3436 women with singleton pregnancies had undergone one or more antenatal OGTT. Among them were 1482 women diagnosed with IGT and delivered in our hospital. There were also 127 women diagnosed with DM who were not included in this analysis. Another 259 women had defaulted and the details on their outcome were not available. As the population served by our hospital is largely southern Chinese, who are generally of shorter stature, the calculation of the BMI would be an appropriate means of relating weight to height. The criterion of >26 kg/m^2 as the definition of high BMI was chosen, following the Institute of Medicine (IOM) recommendation (IOM, 1990) and which has been used in studies examining the effect of maternal obesity and weight gain on pregnancy outcome (Johnson *et al*., 1992; Scholl *et al*., 1995; Edwards *et al*., 1996; Crane *et al*., 1997).

The case notes of the women whose pre-pregnancy BMI were >26 kg/m^2 and whose diagnosis was IGT or normal glucose tolerance were then retrieved for review. There were 394 women (12.4% of the 3177 women who delivered in our hospital) with a pre-pregnancy BMI of >26 kg/m^2 who had either a normal OGTT result (34.0%) or IGT (66.0%). Each subject with IGT and her respective control were matched for the pre-pregnancy BMI (to within 0.1 kg/m^2). The purpose of using controls matched for the exact BMI was to eliminate as far as possible the presence, or to minimize the effects, of other biological variables which might be associated with GDM and which could have influenced pregnancy outcome. This was because these variables might not have been easily identified for adjustment by statistical methods.

Because of the much smaller number of women with normal OGTT results, only 128 women with IGT could be matched with 128 women with normal OGTT results. These cases formed the study and control groups respectively for the final analysis. All the women with IGT were treated with diet restriction only. The two groups were compared for maternal demographic and anthropometric parameters, obstetric complications, mode of delivery and perinatal outcome. Comparison of continuous random variables were made using Student's *t*-test, and percentages were compared using Fisher's exact test. The statistical analysis was performed with a commercial statistical package (Statistics Package for Social Sciences).

Table I. Maternal characteristics and oral glucose tolerance test (OGTT) results in relation to maternal glucose tolerance

	IGT group (n = 128)	Control group (n = 128)	P value
Age (years)	32.9 ± 0.4	30.3 ± 0.4	0.000
Age ⩾35 years (%)	35.2	18.0	0.003
Height (cm)	154.0 ± 0.5	153.3 ± 0.5	NS
Weight (kg)			
pre-pregnant	66.4 ± 0.5	65.7 ± 0.5	NS
pre-delivery	76.3 ± 0.7	75.9 ± 0.7	NS
total gain	9.9 ± 0.4	10.2 ± 0.5	NS
% gain	14.9 ± 0.6	15.7 ± 0.8	NS
Hb (g/dl) booking	12.8 ± 0.1	12.5 ± 0.1	0.040
OGTT (mmol/l) fasting	4.8 ± 0.04	4.4 ± 0.03	0.000
OGTT (mmol/l) 2 h	9.0 ± 0.07	6.6 ± 0.08	0.000
Past history of GDM (%)	7.8	0.8	0.010
Multiparas (%)	65.6	64.1	NS

Results expressed in mean ± SEM except indicated as (%).
IGT = impaired glucose tolerance; Hb = haemoglobin; GDM = gestational diabetes mellitus; NS = not significant.

Results

The pre-pregnancy BMI in the IGT and control groups was 27.9 ± 0.2 (mean ± SEM) kg/m^2. The pre-delivery BMI in the IGT and control groups were 32.1 ± 0.2 kg/m^2 and 32.3 ± 0.2 kg/m^2 respectively (not significant). Despite the similar BMI, the IGT group had higher mean age as well as the proportion with advanced maternal age [⩾35 years, odds ratio (OR) 2.48, 95% confidence interval (CI) 1.39–4.42], but there was no difference in the height, pre-pregnant and pre-delivery weight or weight gain (Table I). The IGT group also had a higher booking haemoglobin. While the OGTT 2 h value was higher as expected, the fasting value was also significantly higher. Although there was no difference in the incidence of multiparous subjects, the incidence of a past history of GDM was higher in the IGT group (OR 10.76, 95% CI 1.36–85.36).

There was no difference in the major antenatal complications, except for urinary infection (OR 9.61, 95% CI 1.20–76.96), in the IGT group (Table II). There was no difference in the incidence of instrumental or Caesarean delivery.

For the infants, there was no difference in the mean gestational age, birthweight or crown–heel length, but the birthweight ratio (birthweight divided by the mean for gestational age) was significantly higher in the IGT group (Table III). As well, the incidences of both LGA (OR 2.21, 95% CI 1.28–3.96) and macrosomic (birthweight ⩾4000 g, OR 3.02, 95% CI 1.05–8.65) infants were higher. While there was no difference in the placental weight, mean Apgar scores, incidence of low Apgar score, perinatal mortality, respiratory and metabolic complications, or sepsis, the incidence of treatment for neonatal jaundice was significantly higher in the IGT group (OR 2.58, 95% CI 1.18–5.68).

Table II. Pregnancy outcome in relation to maternal glucose tolerance

	IGT group (n = 128)	Control group (n = 128)	P value
Pregnancy complications			
ante-partum haemorrhage	10.2	5.5	NS
preterm labour	3.9	2.3	NS
pregnancy-induced hypertension	11.7	10.2	NS
prelabour rupture of membranes	16.4	21.1	NS
urinary tract infection	7.0	0.8	0.019
Delivery			
instrumental	14.1	14.1	NS
Caesarean	25.8	21.1	NS

Results expressed as %.

Table III. Infant outcome in relation to maternal glucose tolerance

	IGT group (n = 128)	Control group (n = 128)	P value
Gestational age (weeks)	38.7 ± 0.2	38.9 ± 0.2	NS
Crown–heel length (cm)	50.6 ± 0.2	50.1 ± 0.2	NS
Birthweight (g)	3335 ± 49	3249 ± 41	NS
>90th percentile[a]	32.8	18.1	0.009
≤10th percentile[a]	3.1	3.9	NS
≥4000 g[a]	10.9	3.9	0.054
Birthweight ratio	1.10 ± 0.012	1.07 ± 0.011	0.044
Placental weight (g)	655 ± 13	635 ± 11	NS
Apgar score at 1 min	8.5 ± 0.1	8.4 ± 0.1	NS
Apgar score at 5 min	9.5 ± 0.09	9.7 ± 0.09	NS
Apgar score <7 at 1 min[a]	10.2	8.6	NS
Apgar score <7 at 5 min[a]	0.8	0.8	NS
Treatment for jaundice[a]	18.0	7.8	0.024
Respiratory complications[a]	5.5	4.3	NS
Metabolic complications[a]	3.9	3.4	NS
Sepsis[a]	7.8	7.1	NS

[a]Results expressed in mean ± SEM or % as indicated.

Discussion

A previous study in our population has demonstrated a relationship between maternal obesity, as indicated by the ponderal index, with the delivery of heavier babies and more infant macrosomia (5.6 versus 2.5%), higher incidence of GDM (13 versus 4.2%), and of Caesarean delivery (Duthie *et al*., 1988). As the presence of GDM alone could account for the increased risk for Caesarean section and macrosomia, which were not influenced by the presence of risk factors (Weeks *et al*., 1994), it was possible that the three-fold higher rate of GDM in the obese mothers in our population was the underlying cause of these outcomes. Nevertheless, in another study (Weeks *et al*., 1994), 12% of the women with GDM were obese with a body weight of >80 kg, and it was unclear as to what extent the presence of obese women had contributed to the increased risk for Caesarean section and macrosomia.

While the clinical significance of IGT may have been disputed (Li *et al*., 1987; Nasrat *et al*., 1994), this condition was nevertheless associated with such outcomes as LGA or macrosomic infants, Caesarean delivery, and complications like hypertension (Al-Shawaf *et al*., 1988; Nord *et al*., 1995; Lao and Lee, 1998). However, in view of the fact that these women were also heavier with higher BMI (Al-Shawaf *et al*., 1988; Nord *et al*., 1995; Lao and Lee, 1998), maternal weight excess could have been the underlying factor for these outcomes. Indeed, one study found that even though obese women with GDM gained less weight in pregnancy than normal or lean women with GDM, the infants in the former group were still heavier than the latter two groups (Algert *et al*., 1985). Furthermore, even moderately obese mothers when compared with age and parity matched normal weight controls had increased incidence of gestational hypertension, Caesarean section, LGA, GDM and infant morbidity (Tilton *et al*., 1989). Excess weight in the mother could therefore have been the more important factor, especially in the case of mild GDM.

In order to clarify the impact, if any, of IGT on the outcome of pregnancy in the overweight women, it is necessary to control for maternal weight or BMI. This is because the occurrence of outcomes such as diabetes, hypertension, and perinatal mortality, increase progressively with increasing maternal BMI (Naeye, 1990; Cnattingius *et al*., 1998). Furthermore, infant size was correlated with maternal BMI but was not influenced by glycaemic control, and it was proposed that the increased fetal growth in GDM may be related more to the metabolic abnormalities associated with obesity than to those associated with well controlled GDM (Jacobson and Cousins, 1989). Such an effect could have played a more important role in women with shorter stature, such as the southern Chinese, whose weight could well be within normal by Western standards but whose BMI was nevertheless increased.

In this study, it is apparent that the majority of our women with a high BMI had impaired glucose tolerance. However, by controlling for the maternal BMI, any difference in the maternal characteristics is likely to be the predisposing factors for, and that in pregnancy outcome is likely to be related to, maternal IGT. Thus this study has shown that while there was no difference in maternal weight, weight gain, or BMI during the course of pregnancy, the IGT group was older with more women at 35 years of age or more. As well, the IGT women had a higher haemoglobin concentration at booking, which might have suggested a better nutritional status, or a higher iron store as reflected in their ferritin concentration (Lao and Tam, 1997). Their fasting glucose concentration was also higher, and despite the similar incidence of multiparae, the incidence of a past history of GDM was significantly higher too. These findings suggested that despite a similar BMI, the women with IGT had had some form of underlying metabolic disturbance that predisposed them to the development of IGT during pregnancy.

Except for the increased incidence of urinary infection, there was no difference in pregnancy complications or mode of delivery in the IGT group. Nevertheless, the birthweight ratio was increased together with the incidence of LGA and macrosomic infants in the IGT group, even though the mean gestational age and birthweight appeared similar. This phenomenon was probably related to the combined effects of a slightly shorter gestational age and higher birthweight in the IGT group. Thus an effect of maternal IGT on the size of the infants was demonstrated in spite of maternal diet restriction.

Although it was possible that the IGT group was not compliant with their diet regime, their pre-delivery weight and BMI, as well as the absolute and percentage weight gain in pregnancy, were no different from the values in the control group. The increased incidence of LGA and macrosomic infants in the IGT group could not therefore be attributed to obesity before pregnancy or excess weight gain during pregnancy. This finding is in agreement with the observed effect of GDM on the risk of infant macrosomia that was independent of other risk factors (Weeks *et al*., 1994). Furthermore, the IGT group had increased incidence of treatment for neonatal jaundice. This was probably a reflection of the presence of neonatal polycythaemia due to maternal diabetes (Mimouni *et al*., 1986), although the cord blood haemoglobin or haematocrit results were not available to support this hypothesis.

The results of this study suggest that the increased risk of some of the outcomes attributed to GDM, such as Caesarean delivery and hypertension, are probably related to associated maternal weight excess or obesity, because women who develop GDM tend to be heavier and more obese. Once corrected for maternal BMI, maternal IGT appears to have minimal influence on the pregnancy complications, and none on the mode of delivery. On the other hand, even mild glucose intolerance in the form of IGT does affect the infant size, despite the normalization of maternal weight gain with diet restriction. It is possible that apart from maternal weight and obesity, other factors that predispose the pregnant women to the development of IGT play important roles in determining the infant outcome. Furthermore studies are warranted to elucidate the factors associated with excess fetal growth in mild glucose intolerance.

References

Alberti, K.G.M.M. and Zimmet, P.Z. (1998) Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. *Diabet. Med*., **15**, 539–553.

Algert, S., Shragg, P. and Hollingsworth, D.R. (1985) Moderate caloric restriction in obese women with gestational diabetes. *Obstet. Gynecol*., **65**, 487–491.

Al-Shawaf, T., Moghraby, S. and Akiel, A. (1988) Does impaired glucose tolerance imply a risk in pregnancy? *Br. J. Obstet. Gynaecol*., **95**, 1036–1041.

Cnattingius, S., Bergstrom, R., Lipworth, L. *et al.* (1998) Pregnancy weight and the risk of adverse pregnancy outcomes. *N. Engl. J. Med*., **338**, 147–152.

Crane, S.S., Wojtowycz, M.A., Dye, T.D. *et al*. (1997) Association between pre-pregnancy obesity and the risk of cesarean delivery. *Obstet. Gynecol*., **89**, 213–216.

Duthie, S.J., Li, D.F.H., To, W.K. *et al*. (1988) Obstetric complications among Chinese parturients with extreme prepregnancy ponderal indices. *Aust. N.Z. J. Obstet. Gynaecol*., **28**, 162–164.

Edwards, L.E., Hellerstedt, W.L., Alton, I.R. *et al*. (1996) Pregnancy complications and birth outcomes in obese and normal-weight women: effects of gestational weight gain. *Obstet. Gynecol*., **87**, 389–394.

Engelgau, M.M., Herman, W.H., Smith, P.J. *et al*. (1995) The epidemiology of diabetes and pregnancy in the U.S., 1988. *Diabetes Care*, **18**, 1029–1033.

Galtier-Dereure, F., Montpeyroux, F., Boulot, P. *et al.* (1995) Weight excess before pregnancy: complications and cost. *Int. J. Obes. Relat. Metab. Disord.*, **19**, 443–448.

Gross, T., Sokol, R.J. and King, K.C. (1980) Obesity in pregnancy: risks and outcome. *Obstet. Gynecol*., **56**, 446–450.

Institute of Medicine: Subcommittee on Nutritional Status and Weight Gain During Pregnancy (1990) *Nutrition During Pregnancy.* National Academy Press, Washington DC.

Jacobson, J.D. and Cousins, L. (1989) A population-based study of maternal and perinatal outcome in patients with gestational diabetes. *Am. J. Obstet. Gynecol*., **161**, 981–986.

Johnson, J.W.C., Longmate, J.A. and Frentzen, B. (1992) Excessive maternal weight and pregnancy outcome. *Am. J. Obstet. Gynecol*., **167**, 353–372.

Lao, T.T. and Tam, K.F. (1997) Maternal serum ferritin and gestational impaired glucose tolerance. *Diabetes Care*, **20**, 1368–1369.

Lao, T.T. and Lee, C.P. (1998) Gestational 'impaired glucose tolerance': should the cut-off be raised to 9 mmol l^{-1}? *Diabet. Med*., **15**, 25–29.

Li, D.F.H., Wong, V.C.W., O'Hoy, K.M.K.Y. *et al*. (1987) Is treatment needed for mild impairment of glucose tolerance in pregnancy? A randomized controlled trial. *Br. J. Obstet. Gynaecol*., **94**, 851–854.

Mimouni, F., Miodovnik, M., Siddiqi, T.A. *et al*. (1986) Neonatal polycythemia in infants of insulin-dependent diabetic mothers. *Obstet. Gynecol*., **68**, 370–372.

Naeye, R.L. (1990) Maternal body weight and pregnancy outcome. *Am. J. Clin. Nutr.*, **52**, 273–279.

Nasrat, A.A., Augensen, K., Abushal, M. *et al*. (1994) The outcome of pregnancy following untreated impaired glucose tolerance. *Int. J. Gynaecol. Obstet.*, **47**, 1–6.

Nord, E., Hanson, U. and Persson, B. (1995) Blood glucose limits in the diagnosis of impaired glucose tolerance during pregnancy. Relation to morbidity. *Acta Obstet. Gynecol. Scand.*, **74**, 589–593.

Scholl, T.O., Hediger, M.L., Schall, J.I. *et al*. (1995) Gestational weight gain, pregnancy outcome, and postpartum weight retention. *Obstet. Gynecol*., **86**, 423–427.

Tilton, Z., Hodgson, M.I., Donoso, E. *et al*. (1989) Complications and outcome of pregnancy in obese women. *Nutrition*, **5**, 95–99.

Weeks, J.W., Major, C.A., de Veciana, M. *et al*. (1994) Gestational diabetes: does the presence of risk factors influence perinatal outcome? *Am. J. Obstet. Gynecol*., **171**, 1003–1007.

World Health Organization Expert Committee on Diabetes Mellitus (1980) *Technical Report Series 646*. World Health Organization, Geneva, pp. 8–12.

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