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Research

Relationship between Positive Glucose Screening, Obesity and Pregnancy Outcome in the Absence of Gestational Diabetes: A Retrospective Cohort Study

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Abstract

Background: Currently pregnant women with abnormal glucose screening test (GCT), performed at 26 - 28 weeks gestation with a subsequent normal glucose tolerance test (GTT) receive routine care. Could these women be at risk of adverse pregnancy? Objective: Compare rate of caesarean section (CS), induction of labour (IOL), macrosomia, admission to special care nursery and neonatal hypoglycaemia. Designs: Retrospective cohort study. Setting: Ipswich Hospital, Ipswich, Queensland. Participants: Pregnant women having had the test at the hospital laboratory. Methods: Charts review of outcome measures including induction of labour, caesarean section, macrosomia, RDS and short-term neonatal morbidity. Results: We reviewed 882 charts (441 cases and 441 controls). There was a higher IOL rate among cases 21.1% versus 16.6% (OR and 95% CI 1.45; 1.03 - 2.06) and a higher CS rate, 30.4 versus 23.6 (OR and 95% CI 1.41; 1.05 - 1.91). Compared to women with BMI 18.5 - 24.9, women with BMI of 30 and above had a significantly higher IOL rate (47.1% versus 22.6%), higher CS rate (47.2% versus 25.7%) and higher rate of macrosomic baby (79.2% versus 4.2%). There were more women amongst the cases who were older, smoked, had a BMI 30 and above and had previous history of GDM. After adjusting for maternal age, BMI and smoking status, there was still an increased odds of CS, IOL and macrosomia, but this did not reach statistical significance. Conclusion: Abnormal glucose screening test in the absence of gestational diabetes is associated with adverse pregnancy outcome. This is largely contributed by maternal obesity.

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1. Introduction

In Queensland, Australia, it is a standard practice for all pregnant women to have a 50 g glucose challenge test (GCT) at 26 - 28 weeks gestation. Those who have an abnormal test (1 hour value 7.8 mmols/l or above) are requested to have a fasting 75 g oral glucose tolerance test (GTT). Women with a fasting value of 7.0 or above or a 2-hour value of 11.1 or above are defined as diabetic and those with fasting 5.5 - 6.9 or a 2-hour value of 7.8 or above and less than 11.1 are defined as gestational diabetics [1].

Currently women who have had an abnormal GCT and a normal GTT receive routine antenatal care. A recent study has shown that there was a statistically significant increase in risk of preeclampsia, caesarean section (CS) and neonatal hypoglycaemia with increasing levels of blood sugar with the GCT [2]. As these findings were based only on the GCT, the group probably included some women who may have developed GDM.

A 10-year audit [3] and a review of a subgroup of the population from the ACTS trial [4] have suggested that women with a positive GCT and a negative GTT may be at increased risk of preeclampsia, CS, hypoglycaemia and hyperbilirubinaemia compared to women with normal GCT. These results do not however appear to have been controlled for any confounding variables.

There has been only one small (150 women in each group) controlled trial [5] that stratified such women by age and BMI and that noted no significant difference between untreated women with positive GCT and negative GTT compared to controls with negative GCT, with regard to CS rate, macrosomia, admission to neonatal intensive care unit or in neonatal hypoglycaemia. There were significantly more newborns with a higher ponderal index among the cases.

Primary objective of our study was to obtain a larger sample size to compare the CS rates in these two groups. Secondary objective was to compare outcomes such as induction of labour (IOL), macrosomia, admission to SCN and neonatal hypoglycaemia and to explore the association between these outcomes and the test status.

2. Methods

This was a retrospective cohort study conducted at Ipswich General Hospital, Ipswich, Queensland from January 2004 to December 2010. The study was approved by the Darling Downs and West Morton Health Service District Human Research Ethics Committee. Eligible women were those who had both their GCT (at 26 - 28 weeks gestational age confirmed at the first booking in visit) and GTT both performed at the Ipswich Hospital Pathology Department. Cases were women who had a positive 50 g GCT and a normal 75 g GTT. For each case the control was the next woman tested at the same laboratory and around the same gestation but with a normal GCT result. Both groups would normally have received the standard care as for non GDM women. Data on pregnancy and birth outcomes were extracted from medical charts.

Differences between the two groups in relation to maternal characteristics were tested using Student's t test for normally distributed continuous data. Differences between proportions for categorical data was tested using Chi-square test, otherwise Fisher's exact test was used when there was a count of 5 or less.

The relationship between test status and each maternal characteristic and pregnancy outcome variable was initially explored using univariate logistic regression. Maternal characteristics found to have a statistically significant relationship with GCT status were incorporated into the multivariate logistic regression models examining the association between GCT status and each of the following variables [IOL, CS, macrosomia (birthweight > 4000 g), admission to special care nursery and neonatal hypoglycaemia].

Statistical significance was set at a two sided p value of <0.05. Stata/SE version 9.0 for Windows (StataCorp LP, College Station, Texas, USA) was used for statistical analysis.

The sample size calculation is based on the hypothesis that there will be a 50% increase in the proportion of women undergoing caesarean section (from an estimated 20% in the control group to 30% in the positive GCT group). A sample size of 882 (441 cases and 441 controls) will provide over 90% power to detect a difference of 50% in the proportion of caesarean sections with an alpha level of 0.5.

3. Results

During the study period we reviewed charts of 882 participants (441 cases and 441 controls). Demographic characteristics of the women in the two groups are shown in **Table 1**. There were significantly more women amongst the cases who were older (mean age 28.6 years versus 26.0 years, p < 0.001), had a BMI of 30 and above (42.8% versus 31.8%, p = 0.007), had previous history of Gestational diabetes (2.7% versus 0.6%, p = 0.064) and were smokers (33.7% versus 26.8%, p = 0.025). There were fewer women amongst the cases who

Table 1. Characteristics of women with positive GCT compared with women with a normal GCT.

Characteristics	Positive GCT (cases) n = 441 (%)	Normal GCT (controls) n = 441 (%)	p value
Maternal age (years)			
Mean ± sd	28.6 ± 6.1	26.0 ± 5.5	<0.000[a]
Missing	0	0	
Gravida			
1	107 (24.4)	117 (26.5)	0.093
Missing	2	0	
Body mass index (kg/m^2)			
<18.5	6 (1.5)	10 (2.5)	
18.5 - 24.9	106 (26.2)	139 (34.2)	
25 - 29.9	119 (29.5)	128 (31.5)	0.007
≥30	173 (42.8)	129 (31.8)	
Missing	37	35	
Smoking	148 (33.7)	118 (26.8)	0.025
Missing	2	0	
Previous gestational diabetes mellitus	9 (2.7)	2 (0.6)	0.064[b]
Missing	108	119	
Previous hypertension	40 (9.1)	35 (7.9)	0.532
Missing	2	0	
Ethnicity			
Caucasian	344 (78.0)	355 (80.5)	
ATSI[*]	18 (4.1)	22 (5.0)	
Samoan	50 (11.3)	45 (10.2)	0.481
Asian	12 (2.7)	10 (2.3)	
Others	17 (3.9)	9 (2.0)	
Marital status			
Never married	58 (13.3)	82 (18.9)	
Married/de facto	371 (84.9)	344 (79.1)	0.075
Divorced/separated	8 (1.8)	9 (2.1)	
Missing	4	6	

[*]Aboriginal and/or Torres Strait Islander; [a]Values are mean ± standard deviation, and the comparisons are mean difference; [b]Fisher's exact.

were never married (13.3% versus 18.9%, overall p = 0.075). About four-fifths of the cases and controls were Caucasian and married or in a de-facto relationship.

Association between glucose status and pregnancy complications and outcomes are shown in **Table 2**. Compared to controls, there was a higher IOL rate among cases 21.1% versus 16.6% (OR 1.45, 95% CI 1.03 - 2.06, p = 0.020) and a higher CS rate, 30.4% versus 23.6% (OR 1.41, 95% CI 1.05 - 1.91, p = 0.023), mostly contributed by failure to progress. None of the others differences were statistically significant. The leading indications for induction of labour were the same for both groups; post dates (40.4%) and spontaneous rupture of membranes (17.5%).

Regardless of GCT status there was an increased odds of IOL (OR 2.24, 95% CI 1.43 - 3.53), CS (OR 1.74, 95% CI 1.18 - 2.55), and macrosomia (birth weight > 4000 g) (OR 16.3, 95% CI 2.17 - 122.6) among obese women compared with women with normal range BMI. There was no significant association between obesity and either neonatal hypoglycaemia or admission to SCN (**Table 3**).

After adjusting for maternal age, BMI and smoking status, a positive GCT was associated with increased odds of IOL (aOR 1.43, 95% CI 0.98 - 2.07), CS (aOR 1.20, 95% CI 0.86 - 1.67) and macrosomia (aOR 2.07, 95% CI 0.83 - 5.20) and a decreased odds of admission to SCN (aOR 0.97, 95% CI 0.62 - 1.52). However none of these associations reached statistical significance (**Table 4**).

4. Discussion

This is the largest study to date showing that women who have an abnormal GCT but a normal GTT, and who are generally treated as low-risk women actually have an increased odds of IOL, CS and macrosomia. However after adjusting for the effect of maternal age, smoking and BMI, these were not statistically significant.

These findings of higher CS rate concur with those from South Australia [2] [4] but we did not show any increased rate of neonatal hypoglycaemia. The South Australian data used blood glucose levels of GCT and probably included women with GDM.

It is of note however that there were significantly more women who had a high BMI, who were older and who smoked amongst the cases. After controlling for these factors, there was still an increased odds of IOL, CS and

Table 2. Association between GCT status and pregnancy outcomes.

	(Cases) n = 441 (%)	(Controls) n = 441 (%)	OR [95% CI]	p value
Pregnancy complications	38 (8.6)	41 (9.3)	0.92 [0.58, 1.46]	0.724
Induction of labour	93 (21.1)	73 (16.6)	1.45 [1.03, 2.06]	0.020
Caesarean section	134 (30.4)	104 (23.6)	1.41 [1.05, 1.91]	0.023
Epidural	62 (14.1)	63 (14.3)	0.98 [0.67, 1.43]	0.923
3rd/4th degree tear	6 (1.4)	6 (1.4)	1.10 [0.35, 3.47]	0.053
Birth weight (grams) Mean ± sd	3495 ± 572	3479 ± 523	1.00 [1.00 - 1.00]	0.680
>4500 (ref: ≤4500 g)	18 (4.1)	9 (2.1)	2.03 [0.90, 4.57]	0.082
Missing	2	5		
Gestational age at birth (weeks) Mean ± sd	39.2 ± 1.5	39.2 ± 1.8	0.99 [0.91 - 1.07]	0.736
<37 weeks (ref: ≥37 wks)	23 (5.2)	23 (5.2)	1.00 [0.55, 1.81]	1.000
>41 weeks (ref: ≤41 wks)	7 (1.6)	6 (1.4)	1.17 [0.39, 3.51]	0.780
5 min Apgar 5 or less	2 (0.5)	1 (0.23)	2.0 [0.18, 22.1]	0.564
Missing	0	1		
Admission to SCN	61 (13.8)	50 (11.4)	1.25 [0.84, 1.87]	0.270
Missing	0	1		
Neonatal hypoglycaemia	11 (2.5)	10 (2.3)	1.10 [0.46, 2.62]	0.825

Table 3. Association between maternal BMI category and selected pregnancy outcomes.

Induction of labour*				
	Yes (n = 155)	No (n = 541)	OR (95% CI)	p value
BMI (kg/m²)				
<18.5	0 (0.0)	12 (2.2)	-	-
18.5 - 24.9	35 (22.6)	185 (34.2)	Referent	-
25 - 29.9	47 (30.3)	172 (31.8)	1.44 (0.89 - 2.34)	0.137
≥30	73 (47.1)	172 (31.8)	2.24 (1.43 - 3.53)	0.000
Caesarean section				
	Yes (n = 214)	No (n = 596)	OR (95% CI)	p value
BMI (kg/m²)				
<18.5	5 (2.3)	11 (1.9)	1.57 (0.52 - 4.71)	0.421
18.5 - 24.9	55 (25.7)	190 (31.9)	Referent	-
25 - 29.9	53 (24.8)	194 (32.6)	0.94 (0.62 - 1.45)	0.791
≥30	101 (47.2)	201 (33.7)	1.74 (1.18 - 2.55)	0.005
Macrosomia (birth weight > 4500 g)				
	Yes (n = 24)	No (n = 780)	OR (95% CI)	p value
BMI (kg/m²)				
<18.5	0 (0.0)	16 (2.1)	-	-
18.5 - 24.9	1 (4.2)	241 (30.9)	Referent	-
25 - 29.9	4 (16.7)	242 (31.0)	3.98 (0.44 - 35.9)	0.218
≥30	19 (79.2)	281 (36.0)	16.3 (2.17 - 122.6)	0.007
Admission to SCN				
	Yes (n = 95)	No (n = 714)	OR (95% CI)	p value
BMI (kg/m²)				
<18.5	3 (3.2)	13 (1.8)	1.72 (0.46 - 6.39)	0.419
18.5 - 24.9	29 (30.5)	216 (30.3)	Referent	-
25 - 29.9	25 (26.3)	221 (31.0)	0.84 (0.48 - 1.49)	0.554
≥30	38 (40.0)	264 (37.0)	1.07 (0.64 - 1.80)	0.791
Neonatal hypoglycaemia				
	Yes (n = 17)	No (n = 793)	OR (95% CI)	p value
BMI (kg/m²)				
<18.5	1 (5.9)	15 (1.9)	2.00 (0.23 - 16.8)	0.534
18.5 - 24.9	8 (47.1)	237 (29.9)	Referent	-
25 - 29.9	3 (17.7)	244 (30.8)	0.36 (0.10 - 1.39)	0.139
≥30	5 (29.4)	297 (37.5)	0.50 (0.16 - 1.54)	0.228

*Analysis excludes women who had no labour.

Table 4. Association between positive GCT status and selected pregnancy outcomes adjusted for maternal age, BMI and smoking status.

Variable	Odds ratio (aOR)[*]	Standard error	p value	95% CI
Caesarean section	1.20	0.20	0.298	0.86 - 1.67
Induction of labour	1.43	0.28	0.060	0.98 - 2.09
Macrosomia (>4500 g)	2.07	0.97	0.119	0.83 - 5.20
Admission to special care nursery	0.97	0.22	0.910	0.62 - 1.52
Neonatal hypoglycaemia	1.00	0.51	0.998	0.37 - 2.71

macrosomia, however the association was not statistically significant. The lack of statistical significance could be due to the sample size (study was not powered to undertake multivariate analysis). These results suggest that although women with positive screening in the absence of GDM have an increased odds of IOL, CS and macrosomia, it is the high BMI, advanced maternal age and smoking that contribute to the trend towards the increased risk of adverse outcomes amongst the cases and that should be of concern in any intervention strategy. GCT may be a marker to alert clinicians to look at other interventions in caring for such women. The association between obesity and adverse pregnancy outcomes is not new. A Danish population-based study [6] of women with raised BMI but normal glucose levels reported that the risk of hypertensive complications, caesarean section, induction of labour and macrosomia was significantly increased in both overweight women and obese women compared with women who were of normal weight. A UK-based study [7] also showed a clear dose dependent association between increasing BMI and macrosomia, the relative risk increasing by 1.7, 2.7 and 4.8 with overweight, obese and morbidly obese women respectively. Others have similarly reported a strong association between BMI and risk of macrosomic baby [8]-[11], and risk of caesarean section [7]-[13] even when women with GDM were excluded [8].

The association between BMI and induction of labour is also not new. Several studies have shown that women with increased BMI are more likely to require IOL [6] [10] [13]. It is not clear why this may be so. Some have noted an increased risk of post dates as the indication [10] but this did not seem to be the case in our cohort. It is possible that women with high BMI have other complications that increase the need for induction of labour, although we were not able to demonstrate this in our study either, but this could be a cascade of events starting with post dates, a difficult induction of labour and eventually other interventions including a caesarean section.

This study clearly demonstrates the need for careful assessment of women who have an abnormal GCT particularly if they happen to be obese. Several recent publications [14]-[16] recommend that all obese pregnant women should be offered advice regarding sensible weight reduction, including diet, exercise and referral to a dietician where appropriate. Despite excluding women with GDM, there is evidence that even lesser degrees of hyperglycaemia may have additional risks of adverse pregnancy outcome as shown by the HAPO study [17]. With the obesity epidemic seen in most well resourced countries (40% of nulliparae's pregnant women in a study from UK [9] were overweight), it is mandatory that more rigorous and well organised interventions become a health priority. Obesity confers an increased life-time risk of type 2 diabetes and potential interventions in pregnancy appearing promising [18]. Whilst these are still relatively short-term benefits ideally, rigorous interventions need to be targeted at a much earlier age, probably from preschool years.

This large cohort study has clearly shown that a pregnant woman with a high BMI and an abnormal GCT is not a low-risk pregnancy and should be referred for additional multidisciplinary care.

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