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Long-term risk of metabolic disorders in gestational diabetes mellitus mothers and offspring.

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Abstract

Background: The incidence of Gestational Diabetes and Mellitus (GDM) is increasing at recent. It was hypothesized that offspring of mothers with GDM may have a relatively high risk for metabolic diseases, but there is still a controversy. Thus, this study aimed to investigate the long-term risk of glucose and lipid metabolic disorders in offspring of GDM mothers.

Methods: GDM mothers (n=467) who gave birth in our department from February 1998 to July 2005 were enrolled and 123 patients were followed up (GDM group). Non-GDM mothers (n=80) admitted were also followed up (non-GDM group). Related clinical parameters of the offspring in both two groups were collected and analysed.

Results: Compared with non-GDM mothers, GDM mothers had significantly higher serum fasting glucose (5.71 ± 0.95 *vs.* 5.3 ± 0.96 mmol/L) and triglyceride level (1.89 ± 0.68 *vs.* 1.68 ± 0.56 mmol/L), and there were more patients with overweight or obesity (33.33% *vs.* 20.0%), waist circumference ≥ 85 cm (39.02% *vs.* 23.75%), fasting glucose ≥ 6.1 mmol/L (28.46% *vs.* 13.75%), diastolic blood pressure ≥ 85 mmHg (18.70% *vs.* 6.25%) and metabolic syndrome (14.63% *vs.* 0.05%) (all Ps<0.05), respectively. The offspring in GDM group had higher serum fasting glucose and triglyceride and the percentage of the offspring with overweight or obesity (26.02% *vs.* 7.50%), fasting glucose ≥ 6.1 mmol/L (9.80% *vs.* 2.50%) and high triglyceride (12.19% *vs.* 3.75%) in GDM group was higher than that in non-GDM group (all Ps<0.05).

Conclusions: The offspring of GDM mothers were prone to develop metabolic disorders including impaired glucose intolerance and hyperlipidemia, thus increasing the risk factors for cardiovascular disease.

Keywords: Follow-up, Gestational diabetes mellitus, Glycometabolism, Lipid metabolism, Offspring.

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Introduction

In recent year, as the lifestyle has changed, the incidence of diabetes mellitus has been both on the increase all over the world, especially in China [1]. Similar trend on the diagnostic rate of Gestational Diabetes Mellitus (GDM) is also observed [2]. GDM is referred to the occurrence of abnormal glucose metabolism at first onset during pregnancy with the prevalence of 1-14% [3]. It is acknowledged that GDM should be considered as a series of metabolic disorders including glucose and lipid metabolism, which needs special attention in clinical practice. GDM mothers may have a high risk for developing DM within 5-10 years after childbirth [4].

Furthermore, the mothers' health is closely associated with the normal growth of the baby and this has become a hot topic in related research field [5]. However, there is still doubt on the role of maternal GDM in the development of diabetes in the offspring. In addition, most of the studies were conducted in western countries and there is lack of evidence in Chinese population [6-9]. Thus, we performed this study, aiming at investigating the long-term incidence of metabolic disorders in the offspring of GDM mothers by comparing with that of non-GDM mothers.

Patients and Methods

Patients

A total of 467 GDM mothers who gave birth in our department from February 1998 to July 2005 were enrolled and 123 patients were followed up (GDM group). Non-GDM mothers (n=560) admitted during the same study period were also included and 80 patents were followed up (non-GDM group). All the patients signed the written informed consent, and our study was approved by the Ethic Committee of our hospital.

GDM was diagnosed according to the diagnostic criteria by IADPSG [10]. All the patients accepted 75 g Oral Glucose Tolerance Test (OGTT) and if serum glucose level was over 1 mmol/l at 0 h, or 10.0 mmol/l at 1 h, or 8.5 mmol/l at 2 h, GDM was diagnosed.

Follow-up

All the mothers and their offspring were regularly followed up by telephone and outpatient visits. The follow-up period ranged 42 days to 14 years. Clinical parameters like blood pressure, height, body weight and Waist Circumference (WC) were recorded. Blood samples were collected and sent for the examination of Fasting Blood Glucose (FBG), insulin, Total Triglyceride (TG), Total Cholesterol (TC), High Density Lipoprotein-Cholesterol (HDL-C) and Low Density Lipoprotein-Cholesterol (LDL-C). OGTT was also administrated. The final follow-up was performed in June 2013. Related clinical parameters of the offspring in both two groups were analysed and compared. Diabetes mellitus was diagnosed as typical clinical manifestations and FBG ≥ 7.0 mmol/L or blood glucose ≥ 11.1mmol/L at 2 h in 75 g OGTT or any time. Impaired Glucose Tolerance (IGT) was diagnosed as normal FBG and 1.1 mmol/L>blood glucose ≥ 7.8mmol/L at 2 h in 75 g OGTT. Abnormal FBG was diagnosed as 6.1-6.9 mmol/L.

Statistical analysis

All the statistical analysis was conducted using SPSS 13.0 software (SPSS Inc. Chicago, IL, USA). The continuous data were presented as mean ± standard deviation and categorical data were as percentage (%). The differences on continuous and categorical data between two groups were tested by independent student t-test and chi-square, respectively. Two tailed P value less than 0.05 was considered to be statistically significant.

Results

GDM mothers had higher risk for metabolic disorders after delivery.

The percentage of patients with abnormal OGTT was 35.77% (44/123) in GDM group and 18.75% (15/80) in non-GDM group (P=0.009) (Table 1). Mothers in GDM group had higher FBG (5.71 ± 0.95 *vs.* 5.3 ± 0.96 mmol/L, P<0.05) and TG level (1.89 ± 0.68 *vs.* 1.68 ± 0.56 mmol/L, P<0.05). However, no statistical differences were found on HDL-C, LDL-C, fasting insulin and TC (all P>0.05) (Table 2). It was also observed that there were more patients with overweight or obesity (33.33% *vs.* 20.0%), WC ≥ 85 cm (39.02% *vs.* 23.75%), FBG ≥ 6.1 mmol/L (28.46% *vs.* 13.75%), diastolic blood pressure ≥ 85 mmHg (18.70% *vs.* 6.25%) and metabolic syndrome (14.63% *vs.* 0.05%) (all Ps<0.05), respectively (Table 3). The incidence of systolic BP ≥ 130 mmHg (5.69% *vs.* 1.25%) and TG ≥ 1.7 mmol/L (13.01% *vs.* 6.25%) was comparable between two groups (both Ps >0.05).

Offspring of GDM mothers were prone to develop abnormal glucose and lipid metabolism in long term.

The offspring in GDM group had higher TG (1.89 ± 0.68 *vs.* 1.48 ± 0.56 mmol/L in 7 years, 1.94 ± 0.72 *vs.* 1.49 ± 0.62 mmol/L in 10 years, 2.06 ± 0.76 *vs.* 1.59 ± 0.64 mmol/L in 14 years, P<0.05) and FBG level (5.01 ± 0.45 *vs.* 4.70 ± 0.47 mmol/L in 7 years, 5.74 ± 0.48 *vs.* 4.82 ± 0.52 mmol/L in 10 years, 5.86 ± 0.51 *vs.* 4.91 ± 0.49 mmol/L in 14 years, P<0.05) (Table 4). The percentage of the offspring with overweight or obesity (26.02% *vs.* 7.50%), FBG ≥ 6.1 mmol/L (9.80% *vs.* 2.50%) and high triglyceride (12.19% *vs.* 3.75%) in GDM group was higher than that in non-GDM group (all Ps<0.05) (Table 5).

Table 1. *GDM mothers had higher incidence of abnormal OGTT than non-GDM mothers.*

	GDM group (n=123)	Non-GDM group (n=80)	χ^2	P value
Abnormal OGTT, n (%)	44 (35.77)	15 (18.75)	6.812	0.009
Normal OGTT, n (%)	79 (64.23)	65 (81.25)		

Table 2. *Laboratory findings between GDM and non-GDM mothers were compared.*

	GDM group (n=123)	Non-GDM group (n=80)	P value
TC, mmol/L	4.67 ± 0.72	4.56 ± 0.67	0.75
TG, mmol/L	1.89 ± 0.68	1.68 ± 0.56	0.03
HDL-C, mmol/L	1.48 ± 0.37	1.39 ± 0.42	0.54
LDL-C, mmol/L	3.31 ± 0.81	3.21 ± 0.82	0.67
Fasting insulin, mu/L	11.84 ± 9.59	10.32 ± 9.75	0.84
FBG, mmol/L	5.71 ± 0.95	5.30 ± 0.96	0.04

Table 3. *The incidence of metabolic syndrome was evaluated between mothers in two groups.*

	GDM group (n=123)	Non-GDM group (n=80)	P value
Overweight or obesity, n (%)	41 (33.33)	16 (20.00)	0.03
WC ≥ 85 cm, n (%)	48 (39.02)	19 (23.75)	0.04
Systolic BP ≥ 130 mmHg, n (%)	7 (5.69)	1 (1.25)	0.15
Diastolic BP ≥ 85 mmHg, n (%)	23 (18.70)	5 (6.25)	0.02

FBG ≥ 6.1 mmol/L, n (%)	35 (28.46)	11 (13.75)	0.04
TG ≥ 1.7 mmol/L, n (%)	16 (13.01)	5 (6.25)	0.06
Metabolic syndrome, n (%)	18 (14.63)	4 (0.05)	0.03

Table 4. *Laboratory findings of the offspring in the 7 year, 10 year and 14 year follow-up.*

Follow-up		GDM group (n=123)	Non-GDM group (n=80)	P value
7 year	TC, mmol/L	3.79 ± 0.62	3.72 ± 0.59	0.07
	TG, mmol/L	1.89 ± 0.68	1.48 ± 0.56	0.04
	HDL-C, mmol/L	1.16 ± 0.37	1.05 ± 0.42	0.06
	FBG, mmol/L	5.01 ± 0.45	4.70 ± 0.47	0.03
10 year	TC, mmol/L	4.12 ± 0.67	3.98 ± 0.61	0.55
	TG, mmol/L	1.94 ± 0.72	1.49 ± 0.62	0.02
	HDL-C, mmol/L	1.08 ± 0.42	0.95 ± 0.44	0.65
	FBG, mmol/L	5.74 ± 0.48	4.82 ± 0.52	0.02
14 year	TC, mmol/L	3.70 ± 0.58	3.58 ± 0.54	0.75
	TG, mmol/L	2.06 ± 0.76	1.59 ± 0.64	0.03
	HDL-C, mmol/L	0.99 ± 0.45	0.94 ± 0.48	0.45
	FBG, mmol/L	5.86 ± 0.51	4.91 ± 0.49	0.04

Table 5. *The overall incidences of metabolic syndrome in the offspring in the final follow-up were compared.*

	GDM group (n=123)	Non-GDM group (n=80)	χ^2	P value
Overweight or obesity, n (%)	33 (26.02)	6 (7.50)	11.66	0.0006
SBP ≥ 130 mmHg, n (%)	4 (3.25)	2 (2.50)	0.044	0.83
DBP ≥ 85 mmHg, n (%)	13 (10.57)	5 (6.25)	1.12	0.29
FBG ≥ 6.1mmol/L, n (%)	12 (9.80)	2 (2.50)	3.97	0.04
TG ≥ 1.7mmol/L, n (%)	15 (12.19)	3 (3.75)	4.145	0.042

Discussions

Diabetes is a chronic disease with a high complication rate [11]. GDM is special type of DM, which needs early diagnosis and treatment [12]. GDM patients may progress into DM after delivery. It was reported that the risk of DM in GDM mothers were greatly higher than that in non-GDM in western countries [13]. However, things may different in China due to the different geographical distribution and lifestyle. Thus, we designed and conducted this prospective cohort study to investigate the long-term risk of metabolic disorders in GDM mothers and their offspring by comparing with that in non-GDM mothers and their offspring. These findings could help deepen the current understanding on GDM and further benefit the optimization of the management of such patients.

In our study, it was observed that the incidence of DM in GDM mothers was higher than that non-GDM mother [14]. Similar trend on the lipid and glucose metabolism disorders was also shown. Previous studies demonstrated that the incidence of DM in GDM mothers was increased year by year, which could reach the peak within 5 years after childbirth and then become stable after 10 years. Our patients were followed for up to 14 years and the yearly peak incidence of DM was 35.77%. In addition, there were a certain percentage of GDM mothers who had abnormal glucose metabolism. For such patients, early monitoring of blood glucose and diet control is suggested, which may prevent the development of DM [15].

Metabolism syndrome is a clinical syndrome characterized as a complex of risk factors for cardiovascular diseases [16]. Such patients may have DM, IGT or insulin resistance complicated with hypertension, lipid disorders, atherosclerosis, proteinuria and overweight or obesity. Metabolism syndrome is a chronic progressive condition associated with multiple risk factors. Most patients diagnosed are at advanced stage, which could be difficult to be cured [17]. Thus, early prevention and immediate treatment is highly recommended for metabolism syndrome. GDM mothers are prone to have obesity, increased fasting insulin, high TG and hypertension [18,19]. Statistical differences were found on TC and FBG level between GDM and non-GDM mothers (both Ps<0.05). These data indicated

that TC, TG and blood pressure should be regularly examined in GDM mothers.

It is well acknowledged that the percentage of children with overweight or obesity is greatly increasing [8]. More and more evidence proved that the health condition of mothers might contribute a lot to the development of obesity in the offspring. Our data also verified that the offspring of GDM mothers had higher TG level than that non-GDM mothers, and overweight and obesity was more common in the offspring of GDM mothers, suggesting that the offspring of GDM mothers have a relatively higher risk for metabolism disorders than that of non-GDM mothers, which might be validated as an independent risk factor. Furthermore, the offspring of GDM mothers could be considered as high risk population for metabolism disorders. There were limitations in this study. First, all the patients were from one single center. Second, the sample size was not quite large. However, a multicenter large-scale investigation will be planned soon.

Taken together, based on our long-term follow-up, GDM mothers and their offspring could have higher risk for glucose and lipid metabolism disorders as well a hypertension and overweight or obesity. GDM could be a risk factor and such patients need to be regularly followed up in order to make early diagnosis and take early preventative measures such as diet control, proper education, physical activity and glucose monitoring.

Compliance with Ethical Standards

Conflicts of interest

There is no conflict of interest.

**Ethical approval*

This study was approved by the Ethic Committee of our hospital. The informed consent was obtained from all the patients.

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No

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