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A Cohort Study of a History of Gestational Diabetes Mellitus and the Risk of Incident Type 2 Diabetes in Louisiana Women

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A COHORT STUDY OF A HISTORY OF GESTATIONAL DIABETES MELLITUS AND THE RISK OF INCIDENT TYPE 2 DIABETES IN LOUISIANA WOMEN

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABBREVIATIONS

ADA	American Diabetes Association
BMI	Body Mass Index
CI	Confidence Interval
GDM	Gestational Diabetes Mellitus
ICD	International Classification of Disease
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance
LSUHCSD	Louisiana State University Health Care Services Division
LSUHLS	Louisiana State University Hospital-Based Longitudinal Study
NDDG	National Diabetes Data Group
OGTT	Oral Glucose Tolerance Test
SE	Standard error
WHO	World Health Organization

ABSTRACT

Gestational diabetes mellitus (GDM) is one of the most common pregnancy complications. It has been shown that a history of GDM is associated with an increased risk of incident type 2 diabetes in women. In this project, we aim to investigate 1) the trend of GDM incidence in Louisiana State University Health Care Services Division (LSUHCSD) hospital system during 1997 to 2009; 2) the race-specific association between a history of GDM and the risk of incident type 2 diabetes and how the risk changes over years after the index pregnancy.

We conducted a retrospective study among women aged 13-50 years. Pregnancies, GDM cases and type 2 diabetes cases were identified by using the International Classification of Disease (ICD) -9 code from the Louisiana State University Hospital-Based Longitudinal Study (LSUHLS) database. The annual incidence of GDM and it standard error (SE) were calculated. Cox proportional hazards regression models were used to estimate the association of a history of GDM with the risk of incident type 2 diabetes. The association between previous GDM and the risk of type 2 diabetes in different postpartum periods was examined using logistic regression.

The incidence of GDM increased in most years from 1997 to 2009 and reached a peak in 2002. The incidence of GDM increased with age and reached the peak at 35-39 years of age. Among the three study races, Asians had a significantly higher incidence of GDM than Whites and African Americans. Between 1990 and 2009, 1,142 GDM women and 18,856 non-GDM women presented their first record of pregnancy in the LSUHLS database. During a mean follow-up of 8.6 years, 1,067 women without a history of GDM and 327 women with a history of GDM developed type 2 diabetes. The multivariable-adjusted (age, smoking, income, postpartum body mass index (BMI), postpartum systolic blood pressure, and race)

hazard ratio of type 2 diabetes suggested that a history of GDM is a strong predictor of subsequent type 2 diabetes among Louisiana women, especially among African American women. In addition, risk of type 2 diabetes was decreased by the time after the index delivery.

INTRODUCTION

Gestational diabetes mellitus (GDM), defined as any degree of glucose intolerance with onset or first recognition during pregnancy,(ADA, 2003) is a major health problem affecting about 7% of pregnancies in the United States.(ADA, 2003) Recent data have shown a substantial rise in the incidence of GDM among White, African American, and Asian women (Dabelea et al., 2005b; Ferrara et al., 2004) along with the increase in the prevalence of obesity (Flegal et al., 2010; Hedley et al., 2004; WHO, 2000). It has been estimated that GDM increased national medical costs by $636 million in 2007 (Chen et al., 2009). Although most women with GDM regain normal glucose tolerance after delivery, many of them are featured with metabolic disorders in postpartum and later life. For instance, women with prior GDM are at increased risk of subsequent type 2 diabetes, impaired glucose tolerance (IGT), obesity, hypertension, dyslipidemia, and the metabolic syndrome (Carr et al., 2006; Flegal et al., 2010; Hedley et al., 2004; Lauenborg et al., 2005; WHO, 2000). Offspring of women with GDM also have increased risk of obesity and diabetes in childhood and early adulthood (Dabelea, 2007). Recently, an increase in the prevalence of GDM was reported in Colorado (Dabelea et al., 2005b) and California (Ferrara et al., 2004), the United States, and in Tianjin(Zhang et al., 2011), China using locally available data.

Type 2 diabetes, a common and serious condition associated with reduced life expectancy and considerable morbidity, has posed a great burden on patients, their families, and health care systems.(ADA, 2011) Several studies have demonstrated that type 2 diabetes can be prevented or delayed by implementing lifestyle modifications (Knowler et al., 2002; Tuomilehto et al., 2001). In order to be cost-effective, lifestyle interventions to prevent or delay type 2 diabetes should be directed toward individuals at increased risk for the disease

(Eddy et al., 2005; Herman et al., 2005). Therefore, it is of great importance to find clinical predictors of type 2 diabetes.

The present study aims to assess the trends in the annual incidence of GDM and the race-specific association between a history of GDM and incidence of type 2 diabetes and to evaluate how the risk changes over years after the index pregnancy by using the well-characterized Louisiana State University Hospital-Based Longitudinal Study (LSUHLS) database.

Justification

Although long-term trends of GDM are available at the national level, they are less clear for population subgroups especially those on middle or low income and also at high risk of obesity. Furthermore, it is also unclear to what extent a history of GDM could predict incident type 2 diabetes in the population of Louisiana which has the fourth highest prevalence of diabetes in the United States and whether there is a racial difference between the association of GDM and type 2 diabetes.

The present study, which is part of the LSUHLS, utilized a cohort design. The subjects involved in this study were women served by Louisiana State University Health Care Services Division (LSUHCSD) hospitals, most of which were from middle or low income families. The present study would provide important information for understanding the scope and burden of GDM and type 2 diabetes in Louisiana women especially those on middle or low income.

Research Questions

1. What is the trend in the annual incidence of GDM in the women served by LSUHCSD hospitals?
2. What is the association between a history of GDM and the risk of incident type 2 diabetes in the women served by LSUHCSD hospitals?

3. What is the racial difference between the associations of GDM and the risk of incident type 2 diabetes in the women served by LSUHCSD hospitals?

Hypotheses

1. The incidence of GDM increased over years in the women served by LSUHCSD hospitals.
2. A history of GDM predicted subsequent type 2 diabetes among the women served by LSUHCSD hospitals.
3. In the LSUHCSD hospital system, African American women with a history of GDM showed a higher relative risk for incident type 2 diabetes than White women with a history of GDM.

Limitations

1. The results of the present study, to be conducted with women from middle or low-income families in Louisiana, will not be generalized to other regions and socio-economic groups in the United States.
2. Even though the analysis used to estimate the association between a history of GDM and type 2 diabetes was adjusted for age, smoking, income, BMI, systolic blood pressure, and race, residual confounding due to the measurement error in the assessment of confounding factors, unmeasured factors such as physical activity, education, dietary factors and a family history of diabetes, were not determined thus, cannot be excluded.

REVIEW OF LITERATURE

GDM

GDM, defined by the American Diabetes Association (ADA) as any degree of glucose intolerance with onset or first recognition during pregnancy, is a major health problem affecting about 7% of pregnancies in the U.S.(ADA, 2003) Recent data have shown a substantial rise in the incidence of GDM among women of various ethnic/racial backgrounds.(Dabelea et al., 2005b; Ferrara et al., 2004) GDM is associated with adverse maternal and fetal outcomes, such as cesarean delivery, embryopathy, birth trauma and fetal macrosomia.(ADA, 2003; Ecker and Greene, 2008) Offspring of women complicated with GDM have increased risk of obesity, glucose intolerance, and diabetes in childhood and early adulthood.(Dabelea, 2007) Also, a history of GDM increases the risk of having subsequent type 2 diabetes and IGT after pregnancy.(Bellamy et al., 2009; Dornhorst and Rossi, 1998; Kim et al., 2002) In addition, women with prior GDM are also at increased risk of cardiovascular disease risk factors, such as obesity, hypertension, dyslipidemia, and the metabolic syndrome.(Carr et al., 2006; Lauenborg et al., 2005) Therefore, studying GDM would facilitate people's understanding on GDM as well as other diseases.

International Criteria for GDM Diagnosis

One critical issue in studying GDM is to understand the different diagnostic criteria of GDM. The major diagnostic criteria of GDM used around the world are listed in Table 1. O'Sullivan, a pioneer in the study of GDM, established the oral glucose tolerance test (OGTT) for assessing the upper limit of glycemic normality in pregnancy in 1964.(O'Sullivan and Mahan, 1964) The O'Sullivan criteria were endorsed by the National Diabetes Data Group (NDDG) in 1979 and were regarded as the most appropriate diagnostic method for GDM. (National Diabetes Data Group, 1979) In 1982, Carpenter and Coustan published new criteria

Table 1. GDM diagnostic criteria

Name, Year	Diagnostic Criteria
WHO, 1985 (WHO, 1985)	2-h 75 g OGTT: (One or more must be met or exceeded.) Fasting: ≥ 140 mg/dl (7.8 mmol/l) 2-h: ≥ 200 mg/dl (11.1 mmol/l)
WHO, 1999 (Alberti and Zimmet, 1998)	2-h 75 g OGTT: (One or more must be met or exceeded.) Fasting: ≥ 126 mg/dl (7.0 mmol/l) 2-h: ≥ 200 mg/dl (11.1 mmol/l) IGT: 2-h: 140-199 mg/dl
NDDG, 1979 (National Diabetes Data Group, 1979)	100 g OGTT: (Two or more must be met or exceeded.) Fasting: ≥ 105 mg/dl (5.8 mmol/l) 1-h: ≥ 190 mg/dl (10.6 mmol/l) 2-h: ≥ 165 mg/dl (9.2 mmol/l) 3-h: ≥ 145 mg/dl (8.1 mmol/l)
O'Sullivan & Mahan, 1964 (O'Sullivan and Mahan, 1964)	100 g OGTT: (Two or more must be met or exceeded.) Fasting: ≥ 104 mg/dl (5.8 mmol/l) 1-h: ≥ 190 mg/dl (10.6 mmol/l) 2-h: ≥ 166 mg/dl (9.2 mmol/l) 3-h: ≥ 140 mg/dl (8.1 mmol/l)
Carpenter & Coustan, 1982 (Carpenter and Coustan, 1982)	100 g OGTT: (Two or more must be met or exceeded.) Fasting: ≥ 95 mg/dl (5.3 mmol/l) 1-h: ≥ 180 mg/dl (10.0 mmol/l) 2-h: ≥ 155 mg/dl (8.6 mmol/l) 3-h: ≥ 140 mg/dl (7.8 mmol/l)
ADA, 2003 (ADA, 2003)	100 g OGTT: (Two or more must be met or exceeded.) Fasting: ≥ 95 mg/dl (5.3 mmol/l) 1-h: ≥ 180 mg/dl (10.0 mmol/l) 2-h: ≥ 155 mg/dl (8.6 mmol/l) 3-h: ≥ 140 mg/dl (7.8 mmol/l) Or 75 g OGTT: (Two or more must be met or exceeded.) Fasting: ≥ 95 mg/dl (5.3 mmol/l) 1-h: ≥ 180 mg/dl (10.0 mmol/l) 2-h: ≥ 155 mg/dl (8.6 mmol/l) Or fasting ≥ 126 mg/dl (7.0 mmol/l) Or a casual ≥ 200 mg/dl (11.1 mmol/l) Or 2-h: ≥ 200 mg/dl (11.1 mmol/l)

Table 1 continued

ADA, 2011	75 g OGTT: (One or more must be met or exceeded.)
(ADA, 2011)	Fasting: ≥ 92 mg/dl (5.1 mmol/l)
	1-h: ≥ 180 mg/dl (10.0 mmol/l)
	2-h: ≥ 153 mg/dl (8.5 mmol/l)
	Or a casual ≥ 200 mg/dl (11.1 mmol/l)
	Or A1C≥6.5%

ADA: American Diabetes Association; NDDG: National Diabetes Data Group;

for GDM based on the same testing procedure but with different thresholds. (Carpenter and Coustan, 1982) There was an adjustment for the threshold because hexokinase method, a more precise enzymatic method than the Somogyi-Nelson method, had developed to evaluate the plasma glucose levels. The diagnostic guidelines for GDM of the ADA were based on these criteria. Of note is that, in 2011, the Hemoglobin A1C test for the diagnosis of GDM was officially accepted by the ADA.(ADA, 2011) The World Health Organization (WHO) used a two step procedure: 2-hour 75 g OGTT to diagnose GDM.(WHO/IDF Consultation, 2006) In 1999, the thresholds were lowered in order to increase the sensitivity in detecting glucose intolerance and have been used ever since. (Alberti and Zimmet, 1998)

Although several studies showed that the above GDM diagnostic criteria have successfully predicted adverse maternal, fetal and neonatal outcomes,(Gokcel et al., 2002; Pennison and Egerman, 2001; Retnakaran et al., 2009; Schmidt et al., 2001) large discrepancies exist in these criteria in their ability to identify women with GDM. (Agarwal et al., 2005; Ferrara et al., 2002) For example, the study conducted by Agarwal et al in 2005 (Agarwal et al., 2005), which aimed to highlight the variation between six well-accepted international GDM diagnostic criteria, showed that GDM prevalence between any two criteria was significantly different. In addition, the capacity of the six criteria to predict adverse pregnancy outcome were also different.(Agarwal et al., 2005) Although it is recognized that diagnostic criteria usually performed better in the population they were

developed in than in a different population because of different population characteristics, the large discrepancies seen in this study suggested that more research is needed to help reach a international consensus on optimal GDM diagnostic criteria.

Worldwide GDM Prevalence

GDM prevalence/incidence data were available for all six WHO regions. The reported prevalence/incidence ranged from 1.7% to 22.3%.(Murgia et al., 2006; Ostlund and Hanson, 2004) The studies which reported GDM prevalence/incidence across at least one year are listed in Table 2. (The studies conducted in the United States are listed in the next section) Among these studies, one study conducted in the South-east Asia region reported the highest GDM prevalence: 14.2%, followed by the study conducted in the Eastern Mediterranean region which reported a GDM incidence of 13.5%. The prevalence of the Western Pacific region only ranged from 2.6%-3.8%, which is similar with the reported prevalence in most of the studies conducted in the European region. The reason might be that the Pacific islands were not represented in this region. Underrepresentation was also a problem in the other 5 regions. Moreover, different criteria were used to diagnose GDM in these studies which make it difficult to make comparison between studies and few population based studies were available. Therefore, in order to clearly understand the economic burden caused by GDM, future studies are needed to make the exact magnitude of GDM prevalence clear.

GDM Prevalence in the United States

GDM prevalence data were available for 17 states in the United States: Alaska,(Murphy et al., 1993) California,(Esakoff et al., 2005a) (Ferrara et al., 2004) (Lawrence et al., 2008) Colorado,(Dabelea et al., 2005a) Georgia,(Cho, 2008) Hawaii,(Pedula et al., 2009) Illinois,(Dooley et al., 1991) Indiana,(Indiana State Department of Health, 2009) Montana,(Taryn Hall et al., 2008) Nebraska, (Rettig, 2003) New York, (Rosenberg et al., 2005a) North Carolina,(Jung, 2008) (Thorpe et al., 2005) Oklahoma, (Page, 2003) Oregon,

Table 2. Worldwide prevalence/incidence of GDM

WHO Region	Country	Study period (years)	GDM Prevalence/incidence (%)	Sample Size	Diagnostic Criteria
Americas	Brazil (Schmidt et al., 2000)	1991-1995	7.6	5,004	WHO
	Canada (Aljohani et al., 2008)	2000-2004	3.7	71,527	NDDG
Europe	Netherlands (Weijers et al., 1998)	1992-1997	2	1,640	WHO
	Sweden (Aberg et al., 2002)	1991-1999	2.5	12,382	WHO
	Italy (Di Cianni et al., 2003)	1995-2001	8.7	3,950	Carpenter & Coustan
	Denmark (Jensen et al., 2003)	1999-2000	2.4	5,235	WHO
	Sweden (Ostlund and Hanson, 2004)	1994-1996	1.7	3,616	WHO
	Finland (Poyhonen-Alho et al., 2005)	1996-1998	2.8	523	Carpenter & Coustan
	Switzerland (Noussitou et al., 2005)	2000-2002	2.7	5,788	NDDG
	Turkey (Tanir et al., 2005)	1995-2004	3.1	3,548	Carpenter & Coustan
Eastern Mediterranean	Bahrain (Al Mahroos et al., 2005)	2001-2002	13.5	10,495	Carpenter & Coustan
South-east Asia	China (Ko et al., 2002)	1990-1994	14.2	942	WHO
	Japan (Maegawa et al., 2003)	1999-2001	2.9	749	ADA
	India (Zargar et al., 2004)	1999-2002	3.8	1,000	Carpenter & Coustan
	Pakistan (Chandna et al., 2006)	2003-2004	8.5	633	ADA
	China (Zhang et al., 2011)	1999-2008	4.9	105,473	WHO
Western Pacific	New Zealand (Yapa and Simmons, 2000)	1994-1995	2.6	4,885	Carpenter & Coustan
	Australia (Anna et al., 2008)	1995-2005	3.8	950,747	Australian Criteria

(Lockwood, 2008) Pennsylvania, (Pennsylvania Department of Health, 2010) Texas,(Ramadhani et al., 2004) Utah, (Barnard and Bloebaum., 2003) and West Virginia,(Wise and Taylor, 2002). The state that reported the highest GDM prevalence is Texas (7.9% 2001), while the state that reported the lowest GDM prevalence is Indiana (0.8% in 2008). The differences in the GDM prevalence might be partly explained by the different race/ethnicity composition and the different age composition of the study samples in these studies. Since some of the studies were not performed on a state representative sample, the studies were not conducted during the same period and prevalence data are still lacking in 33 states, further studies are needed to understand the magnitude of GDM across the United States.

In the studies that explored the race/ethnicity difference in the prevalence of GDM in the Unites States, most studies indentified Asian as the race with the highest GDM prevalence followed by Hispanic then African American and White.(Berkowitz et al., 1992; Dabelea et al., 2005b; Esakoff et al., 2005b; Getahun et al., 2008a; Green et al., 1990; Kieffer et al., 2001; Rosenberg et al., 2005b; Savitz et al., 2008; Shen et al., 2005; Thorpe et al., 2005) Only one study reported a lower GDM prevalence in Hispanic than in White, while two studies showed a higher GDM prevalence in White than in African American. Higher adiposity per unit BMI, poor medical care, short stature and genetic factors may contribute to the higher GDM incidence in Asians.(Anastasiou et al., 1998; Chu et al., 2009; Groop and Orho-Melander, 2001; Jang et al., 1998; WHO expert consultation, 2004)

The studies which provided the trends of GDM prevalence/incidence are listed in Table 3. Among all of the studies there was a trend of increasing prevalence/incidence across time with the relative increase ranging from 10% to 121%. Factors such as the diagnosis criteria, the geographic location, the length of the study, and the changing demographics of

Table 3. Change of GDM prevalence/incidence in the United States

Setting	Study period (years)	Change of GDM Prevalence/incidence (%)	Relative increase in GDM prevelance/incidence (%)	Sample Size	Diagnostic Criteria
United States (Getahun et al., 2008a)	1989-2004	1.9-4.2	121	58,922,266	ADA (1997)/ADA (1997) /ADA (2000)
Utah (Barnard and Bloebaum., 2003)	1990-2001	1.4-2.3	64	NA	NA
New York City (Thorpe et al., 2005)	1990-2001	2.6-3.8	46	125,663-110,340	NA
Northern California (Ferrara et al., 2004)	1991-2000	5.1-6.9	35	21,655-30,135	ADA (2000)
Colorado (Dabelea et al., 2005b)	1994-2002	2.1-4.1	95	3,644-4,079	NDDG
Montana (Taryn Hall et al., 2008)	1995-2006	2.2-2.8	27	NA	NA
Southern California (Lawrence et al., 2008)	1999-2005	7.1-7.8	10	32,089-28,321	ADA (2004)

the study samples may contribute to the difference in the estimates. Of note, none of these studies focused on a middle or low income population.

History of GDM and Type 2 Diabetes Risk

The effect of previous GDM on subsequent type 2 diabetes has been studied extensively worldwide (Albareda et al., 2003; Chodick et al., 2010; Feig et al., 2008; Gunderson et al., 2007; Krishnaveni et al., 2007; Lee et al., 2007; O'Sullivan, 1991). These studies consistently recognized GDM as an important risk factor for subsequent type 2 diabetes. One early meta-analysis of six controlled follow-up studies has indicated that the overall relative risk for developing diabetes after GDM was 6.0 (Cheung and Byth, 2003). In the more recent meta-analysis of 20 cohort studies (Bellamy et al., 2009), women with a history of GDM were associated with at least a seven-fold increased risk of incident type 2 diabetes.

In light of a growing body of evidence, it is generally accepted that the progression to type 2 diabetes of parous women with previous GDM is faster than that of parous women without previous GDM (Albareda et al., 2003; Bellamy et al., 2009; Cheung and Byth, 2003; Chodick et al., 2010; Di Cianni et al., 2010; Feig et al., 2008; Kim et al., 2002; Lee et al., 2007; O'Sullivan, 1991). However, the exact mechanism linking GDM to type 2 diabetes is not well understood. Because GDM and type 2 diabetes share the same risk factors such as obesity, physical inactivity, advanced age, ethnic group and family history of diabetes, and the two conditions are strongly associated with each other, GDM and type 2 diabetes are now regarded to share a common genetic background more than ever before (Cho et al., 2009; Di Cianni et al., 2010; Lauenborg et al., 2009). This hypothesis was confirmed by two recent studies which showed that women with previous GDM more frequently display some alleles associated with the high risk of type 2 diabetes (Cho et al., 2009; Lauenborg et al., 2009). Since several intervention studies have showed that it is possible to delay or prevent the

development of type 2 diabetes among those at high risk (Knowler et al., 2002; Tuomilehto et al., 2001), and a recent clinic trial (Ratner et al., 2008) proved that women with a history of GDM who remained at a high risk of developing diabetes benefited from either lifestyle or pharmacologic interventions, determining the true risk of type 2 diabetes in women with a history of GDM and researching into the mechanism behind this association will continue to be important.

METHODS

Subjects

LSUHCSD operates 7 public hospitals and affiliated clinics in different areas in Louisiana which provide quality medical care to residents of Louisiana, regardless of their income or insurance coverage. Overall, LSUHCSD facilities have served about 1.6 million unique patients (35% of the Louisiana population) since 1990. In the population served by the LSUHCSD hospitals, about 46% of patients qualify for free care (by virtue of being low income and uninsured), about 10% of patients are self-pay (uninsured, but incomes not low enough to qualify for free care), about 20% of patients are covered by Medicaid, about 14% of patients have Medicare, and about 10% of patients are covered by commercial insurance. The LSUHCSD, the division responsible for the management of the LSUHCSD facilities, has access to the administrative, anthropometric, laboratory, and the clinical diagnosis data collected at these facilities. All these data are available in electronic form since 1990 for both inpatients and outpatients (the LSUHCSD Disease Management Evaluation Database). Using these data, we have set up the LSUHLS database to follow patients with major chronic diseases. Patients' information on birth date, race, sex, address, types of insurance, family income, smoking habits, date of examination, measurements of height, weight and blood pressure for each visit, diagnosis of various diseases and date of diagnosis, laboratory tests, and medication history were all included in the LSUHLS database. The cohort of pregnancies, which is part of the LSUHLS Study, was identified through the LSUHLS database between January 1, 1990, and December 31, 2009. After excluding participants with incomplete data on any required variables, the trend analyses include a total of 2,751 GDM incident cases among 62,685 pregnancies between 1997 and 2009. After excluding participants with a history of diabetes at baseline and participants with incomplete data on any required variables,

the association analyses include 1,142 women with a history of GDM and 18,856 women without a history of GDM who presented their first record of pregnancy in the LSUHLS database between 1990 and 2009. The study was approved by both Pennington Biomedical Research Center and LSU Health Sciences Center Institutional Review Boards.

Assessments

The gestational women's characteristics, such as age, race-ethnicity, postpartum blood pressure， postpartum BMI, smoking status, and family income, date of pregnancy, and reproductive history were also extracted from the computerized hospitalization records. In the LSUHLS dataset, race-ethnicity was classified as White, African American, Asian, Hispanic, American Indian, native Hawaiian or Pacific Islander, other, and unknown. In the trend analyses, maternal age was categorized as 15.0-19.9, 20.0-24.9, 25.0-29.9, 30.0-34.9, 35.0-39.9, and 40.0-50.0 years. The analyses by race-ethnicity specific incidence were restricted to the White, African American and Asian because the sample sizes of other races are too small (e.g. 229 for American Indian) for meaningful analyses (i.e. stratified by age and year). In the association analyses, maternal age was categorized as 13.0-29.9, 30.0-49.9, and 40.0-50.0 years. The analyses were restricted to the White, African American, Asian, Hispanic, and American Indian. Smoking information was recorded as yes or no based on the answers to the question: "Have you used tobacco in the past 30 days?" Family income was categorized into quartile, ranked from the lowest to the highest. BMI was categorized into normal (<25.0 kg/m^2), overweight (<25.0-29.9 kg/m^2) and obesity (≥30.0 kg/m^2).

Ascertainment of Pregnancy and GDM

Only the first record of pregnancy diagnosis and GDM diagnosis of women aged 13-50 years were included in the present analyses due to the design of cohort study. Pregnancies were identified by using the Ninth Revision of the International Classification of Disease

(ICD) Code v22, v72.42, v23 and 761.5 (ICD-9). GDM cases were identified by using the ICD-9 code 648.8.

Screening and Testing of GDM

Since 1990, all LSUHCSD hospitals have routinely screened for GDM in all non-diabetic pregnancies using a two-step standard protocol. At 24–28 weeks, all pregnant women including women with previously diagnosed diabetes were offered screening for GDM with a 50-g 1-hour OGTT. If pregnant women had a value ≥140 mg/dl, they 1) underwent a 100-g 3-hour or a 75-g 2-hour OGTT; 2) had fasting plasma glucose measured, or 3) had 2-hour postprandial or random plasma glucose levels measured.

Validation of GDM

We conducted a validation study on GDM cases among those who had the laboratory-documented hyperglycemia identified during pregnancy. The laboratory data were used to validate the GDM cases identified by using the ICD-9 code 648.8. Hyperglycemia was defined as follows: 1) at least 2 plasma glucose measurements during a 100-g 3-hour or a 75-g 2-hour OGTT equal or greater than the cutoffs recommended by the ADA (fasting ≥95 mg/dL; 1-hour ≥180 mg/dL; 2-hour ≥155 mg/dL; 3-hour ≥40 mg/dL);(ADA, 2003) 2) 2-hour plasma glucose or random plasma glucose concentration ≥200 mg/dL according to the WHO (WHO Consultation, 1999) and ADA recommendation (Genuth et al., 2003); or 3) fasting plasma glucose ≥126 mg/dL, 2-hour plasma glucose after a 75-g OGTT between 140 and 199 mg/dL (IGT), or fasting plasma glucose between 110 (from 1997 to 2003)/100 (from 2003) and 125 mg/dL (impaired fasting glucose [IFG]) according to WHO (WHO Consultation, 1999) and ADA criteria (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997; Genuth et al., 2003). Plasma glucose testing results were extracted from the LSUHCSD Disease Management Evaluation Database laboratory database, which captures

the results of all laboratory tests performed at all LSUHCSD facilities. All the plasma glucose measurements were performed by using the hexokinase method at each facility's laboratory.

Prospective Follow-up

Follow-up information was obtained from the LSUHLS database by using the unique number assigned to every patient who visits the LSUHCSD hospitals. ICD-9 Code 250.*0 and 250.*2 were used to identify type 2 diabetes cases during follow-up. Since 1990, LSUHCSD's internal diabetes disease management guidelines call for physician confirmation of diabetes diagnoses by applying the ADA(Genuth et al., 2003) or the WHO criteria(Alberti and Zimmet, 1998): a fasting plasma glucose level ≥140 mg/dL (≥126 mg/dL from 1998); 2-hour glucose level ≥200 mg/dL after a 75-g 2-hour OGTT; one or more classic symptoms plus a random plasma glucose level ≥200 mg/dL. Follow-up of each cohort member continued until the date of the diagnosis of type 2 diabetes, the date of the last visit if the subject stopped using LSUHCSD hospitals, or May 31st, 2010.

Statistical Analyses

The number of pregnancies and GDM cases of each study years among each age group were reported. The yearly age-specific incidence of GDM and the yearly race-ethnicity-specific incidence of GDM were calculated by using General Linear Model (logistic regression). The linear trend in incidence across time was tested using incidence GDM as the outcome variable and year as a continuous variable in the model after adjustment for age. The age-standardized incidence was calculated by the direct method to the year 2000 Census population using the age groups 15.0-19.9, 20.0-24.9, 25.0-29.9, 30.0-34.9, 35.0-39.9, and 40.0-50.0 years.(U.S.CensusBureau, 2000)

Differences in risk factors at baseline of GDM women and non-GDM women were tested using General Linear Model after adjustment for age. Cox proportional hazards regression models were used to estimate overall the association of a history of GDM with the

risk of incident type 2 diabetes. The analyses were first carried out adjusting for age, and further for smoking, income, BMI, systolic blood pressure, and race. The association between a history of GDM and the risk of type 2 diabetes in different postpartum periods was examined using logistic regression with adjustment for the above confounding factors. Postpartum year was categorized as <1, 1.0-3.9, 4.0-5.9, 6.0-7.9, 8.0-9.9, and ≥10.0 years. Statistical significance was considered to be $P < 0.05$. Statistical analyses were performed with PASW for Windows, version 19.0 (IBM SPSS Inc, Chicago, III) or SAS for Windows, version 9.12 (SAS Institute, Cary, NC).

RESULTS AND DISCUSSION

Results

GDM Incidence in Louisiana

Table 4 shows the number of pregnancies and GDM cases by years and age groups. From 1997 to 2009, 62,685 women aged 15-50 years with their first record of pregnancy were identified. Among them, a total of 2,751 women had pregnancies complicated by GDM. The mean age of pregnancy was 24.3 ± 0.02 (standard error [SE]) years and did not change by year.

The annual incidence of GDM by age groups is presented in Table 5. The crude incidence of GDM increased from 4.1% (SE 0.3) in 1997 to 5.3% (SE 0.3) in 2002 (increased by 29.3%) and then declined from 4.8% (SE 0.3) in 2003 to 4.4% (SE 0.4) in 2009. Exclusion of the women who were diagnosed with diabetes before they were diagnosed with GDM did not appreciably change the observed trend: the crude incidence of GDM increased from 4.0% (SE 0.2) in 1997 to 4.8% (SE 0.3) in 2002 (increased by 20%) and then declined from 4.4% (SE 0.3) in 2003 to 4.2% (SE 0.4) in 2009. The age-standardized incidence of GDM increased from 5.8% in 1997 to 8.3% in 2002 (increased by 29.3%) and then changed from 6.7% in 2003 to 7.5% in 2009. The total crude and age-standardized average incidences of GDM were 4.4% and 6.3%, respectively. The incidence of GDM increased with age and reached the peak at 35-39 years of age (9.1%) and then decreased in women who were 40-50 years old (7.4%). Compared with women aged 15-19 years, women aged 30-34 years had 2.6 times higher risk of GDM, and women aged 35-39 had 2.9 times higher risk of GDM. The trend of GDM incidence in the six age groups did not change appreciably (all $p > 0.1$).

Table 4. Number of first time pregnancies and incidence of GDM by age and year in the LSUHCSD Hospitals from 1997 to 2009*

Age groups	Year of first pregnant													
(yrs)	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total
No. of first time pregnancies														
15-20	2029	2783	2079	2239	1923	1597	1348	963	714	480	681	698	592	18126
20-24	2308	2950	2236	2427	2217	1840	1687	1303	999	772	1003	966	958	21666
25-29	1233	1530	1212	1271	1088	926	842	688	581	429	605	563	500	11468
30-34	780	918	707	753	668	523	487	370	276	259	313	293	252	6599
35-39	365	451	408	427	338	326	284	175	174	132	158	142	130	3510
40-50	121	161	101	140	141	142	122	88	62	44	69	73	52	1316
Total	6836	8793	6743	7257	6375	5354	4770	3587	2806	2116	2829	2735	2484	62685
No. of incident GDM														
15-20	47	66	36	48	39	52	32	17	16	9	12	13	11	398
20-24	72	77	80	90	73	65	70	56	38	27	24	32	31	735
25-29	65	66	70	77	62	66	49	33	33	31	38	43	31	664
30-34	62	69	48	56	65	44	42	44	25	17	24	21	18	535
35-39	24	35	39	40	25	42	29	12	18	14	13	17	13	321
40-50	9	6	8	14	9	15	9	5	4	2	5	6	6	98
Total	279	319	281	325	273	284	231	167	134	100	116	132	110	2751

*GDM: gestational diabetes mellitus; LSUHCSD: Louisiana State University Health Care Services Division.

Table 5. Incidence (%) of GDM by age and year in the LSUHCSD Hospitals from 1997 to 2009*

Age groups	Year of first pregnant															P value
(yrs)	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total	Adjusted total†	
15-19	2.3	2.4	1.7	2.1	2.0	3.3	2.4	1.8	2.2	1.9	1.8	1.9	1.9	2.2	2.3 (0.2)	0.31
	(0.4)	(0.4)	(0.4)	(0.4)	(0.5)	(0.6)	(0.6)	(0.7)	(0.8)	(1.0)	(0.8)	(0.8)	(0.8)	(0.2)		
20-24	3.1	2.6	3.6	3.7	3.3	3.5	4.1	4.3	3.8	3.5	2.4	3.3	3.2	3.4	3.4 (0.1)	0.15
	(0.4)	(0.3)	(0.4)	(0.4)	(0.4)	(0.5)	(0.5)	(0.6)	(0.7)	(0.8)	(0.6)	(0.7)	(0.7)	(0.1)		
25-29	5.3	4.3	5.8	6.1	5.7	7.1	5.8	4.8	5.7	7.2	6.3	7.6	6.2	5.8	5.7 (0.2)	0.16
	(0.6)	(0.5)	(0.6)	(0.6)	(0.6)	(0.7)	(0.7)	(0.8)	(0.9)	(1.0)	(0.8)	(0.9)	(0.9)	(0.2)		
30-34	7.9	7.5	6.8	7.4	9.7	8.4	8.6	11.9	9.1	6.6	7.7	7.2	7.1	8.1	8.0 (0.3)	0.29
	(0.7)	(0.6)	(0.8)	(0.8)	(0.8)	(1.0)	(1.0)	(1.1)	(1.3)	(0.3)	(1.1)	(1.2)	(1.3)	(0.3)		
35-39	6.6	7.8	9.6	9.4	7.4	12.9	10.2	6.9	10.3	10.6	8.2	12.0	10.0	9.1	9.1 (0.3)	0.27
	(1.0)	(0.9)	(1.0)	(1.0)	(1.1)	(1.2)	(1.3)	(1.6)	(1.6)	(1.8)	(1.6)	(1. 8)	(1.8)	(0.3)		
40-50	7.4	3.7	7.9	10.0	6.4	10.6	7.4	5.7	6.5	4.5	7.2	8.2	11.5	7.4	7.5 (0.6)	0.69
	(1.8)	(1.5)	(2.0)	(1.7)	(1.7)	(1.9)	(1.9)	(2.2)	(2.7)	(3.2)	(2.4)	(2.5)	(2.8)	(0.6)		
Total	4.1	3.6	4.2	4.5	4.3	5.3	4.8	4.7	4.8	4.7	4.1	4.8	4.4	4.4		0.017
	(0.3)	(0.2)	(0.3)	(0.2)	(0.3)	(0.3)	(0.3)	(0.3)	(0.4)	(0.5)	(0.4)	(0.4)	(0.4)	(0.1)		
Age-standardized‡	5.8	4.7	6.4	5.9	5.9	8.3	6.7	5.9	6.4	5.6	6.0	7.1	7.5	6.3		0.019

*Data are given as percentage (SE); GDM: gestational diabetes mellitus; LSUHCSD: Louisiana State University Health Care Services Division.
†Adjusted for race and year.
‡Age adjusted by the direct method to the year 2000 Census population using the age groups 15-19, 20-24, 25-29, 30-34, 35-39, and 40-50 years.

The annual race-ethnicity-specific incidence of GDM is presented in Table 6. Overall, Asian women had a significantly higher age-standardized incidence of GDM (8.6%, P<0.001) than White women (6.7%) and African American women (5.4%).

To assess the accuracy in defining GDM based on ICD 648.8 (ICD 9) in the LSUHLS database, we conducted a validation by using the plasma glucose testing results extracted from our laboratory database. Of the 2,751 GDM women who were diagnosed with GDM by using ICD 648.8, 1,536 GDM women that had electronic records of glucose testing values (the electronic records of glucose testing values were available from 2002). This validation was conducted among the 1,536 GDM women. Of the 1,536 women, 1,158 (75.4%) had GDM by using ADA GDM or diabetes diagnosis criteria.(ADA, 2003; Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997; Genuth et al., 2003), 103 (6.7%) had IGT, and 66 (4.3%) had IFG by using WHO (WHO Consultation, 1999) or ADA diabetes diagnosis criteria (Expert Committee on the Diagnosis and Classification of Diabetes Mellitus, 1997; Genuth et al., 2003) (Figure 1). In LSUHCSD, pregnancies complicated with IGT and IFG were also defined as GDM. Therefore, the agreement between the laboratory tests and the ICD diagnoses was 86.4% for the GDM cases.

History of GDM and the Risk of Incident Type 2 Diabetes

From 1990 to 2009, 19,998 women aged 13-50 years with their first record of pregnancy were identified from LSUHLS database. Among them, a total of 1,142 women had pregnancies that were complicated by GDM. During a mean follow-up of 8.6 years, 1,067 women without a history of GDM and 327 women with a history of GDM developed diabetes. The general characteristics of the study population at baseline by GDM status are presented in table 7. After adjustment for age, GDM women had significantly higher average postpartum BMI and systolic blood pressure when compared with non-GDM women.

Table 6. Annual race/ethnicity-specific incidence (%) of GDM in the LSUHCSD Hospitals from 1997 to 2009*

Year pregnant	White		African American		Asian		P value
	N/N†	Incidence	N/N†	Incidence	N/N†	Incidence	
1997	64/1580	4.1 (0.5)	189/4884	3.9 (0.3)	6/71	8.5 (0.2)	0.14
1998	69/2007	3.4 (0.4)	222/6300	3.5 (0.2)	6/90	6.7 (0.2)	0.27
1999	68/1632	4.2 (0.5)	189/4704	4.0 (0.3)	8/67	11.9 (2.4)	0.005
2000	91/1896	4.8 (0.5)	198/4833	4.1 (0.3)	4/80	5.0 (0.2)	0.42
2001	72/1543	4.7 (0.5)	159/4336	3.7 (0.3)	6/75	8.0 (2.3)	0.045
2002	72/1308	5.5 (0.6)	169/3531	4.8 (0.4)	4/66	6.1 (2.8)	0.55
2003	56/1125	5.0 (0.6)	120/3097	3.9 (0.4)	9/53	17.0 (2.9)	<0.001
2004	34/864	3.9 (0.7)	79/2169	3.6 (0.5)	5/58	8.6 (2.8)	0.14
2005	24/716	3.4 (0.8)	56/1541	3.6 (0.5)	4/54	7.4 (2.9)	0.31
2006	25/657	3.8 (0.8)	30/986	3.0 (0.7)	6/40	15.0 (3.3)	<0.001
2007	41/828	5.0 (0.7)	37/1350	2.7 (0.5)	0/30	0	0.014
2008	60/742	8.1 (0.8)	39/1506	2.6 (0.6)	0/20	0	<0.001
2009	38/746	5.1 (0.8)	43/1351	3.2 (0.6)	3/20	15.0 (4.6)	0.004
Total	714/15,644	4.6 (0.2)	1530/40,588	3.8 (0.1)	61/724	8.4 (0.8)	<0.001
Age-standardized‡	714/15,644	6.7	1530/40,588	5.4	61/724	8.6	<0.001
P value (trend)	<0.001		<0.001		0.18		

*Data are given as percentage (SE); GDM: gestational diabetes mellitus; LSUHCSD: Louisiana State University Health Care Services Division.
†Number of gestational diabetes mellitus/number of first time pregnancies.
‡Age adjusted by the direct method to the year 2000 Census population using the age groups 15-19, 20-24, 25-29, 30-34, 35-39, and 40-50 years.

Table 7. Baseline and follow-up characteristics of women with and without previously diagnosed GDM who delivered a baby in LSUHCSD hospitals*

Characteristics	Non-GDM women	GDM women	P value for trend
Participants, n	18,856	1,142	
Incident DM case, n	1,067	327	
Gestational age, y	24.3 (0.0)	26.8 (0.2)	<0.001
Postpartum BMI, kg/m2	41.1 (0.4)	48.2 (1.7)	<0.001
Postpartum systolic blood pressure, mmHg	128 (0.1)	131 (0.6)	<0.001
Postpartum diastolic blood pressure, mmHg	76 (0.1)	76 (0.4)	0.24
Current smoker, %	19.5	17.9	0.18
Annual family income, $	21,049 (452)	24,494 (1747)	0.056

*GDM: gestational diabetes mellitus, LSUHCSD: Louisiana State University Health Care Services Division, DM: diabetes mellitus. Data are means (SD) unless otherwise indicated; all data, except age, adjusted for age.

In age-adjusted analysis, women with a history of GDM had 7.02 (95% confidence interval [CI] 6.18-7.96) times higher risk of type 2 diabetes compared with non-GDM women (Table 8). Additional adjustment for smoking, income, BMI, systolic blood pressure and race did not appreciably alter the results. Stratification by age, race, and BMI gave similar results (Table 8).

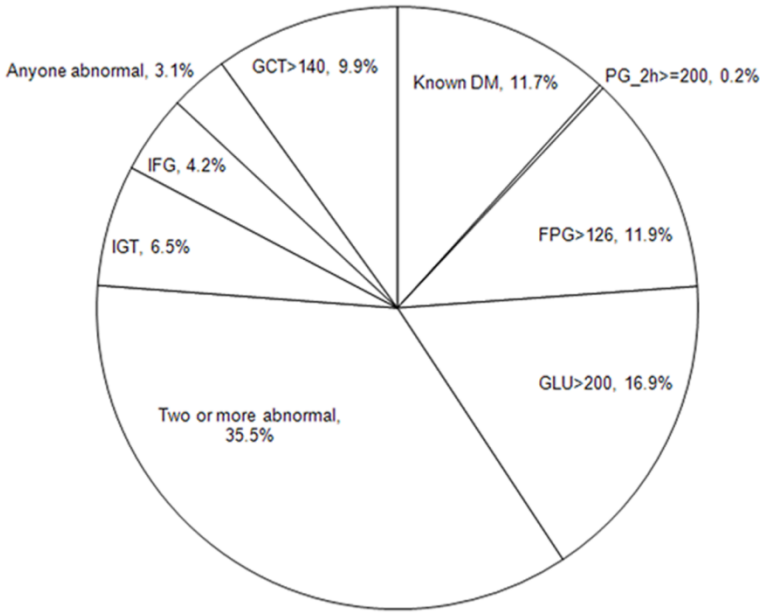

Figure 1. Incidence (%) of GDM (ICD-9:648.8) based on different glucoses levels and diagnosed criteria in the Louisiana State University Health Care Services Division Hospitals from 1997 to 2009. (GDM, gestational diabetes mellitus; Known DM, known diabetes mellitus; PG_2h, 2-hour plasma glucose by OGTT; FPG, fasting plasma glucose; GLU, random plasma glucose; IGT, impaired glucose tolerance; IFG, impaired fasting glucose; OGTT, oral glucose tolerance test; GCT, glucose challenge test)

Table 8. Hazard rations for type 2 diabetes according to GDM status for total study samples and stratified by age, BMI and race*

	No. of case / No. of sample		Person-years		Hazard ratios (95% CIs)		P value for trend	P for interaction
	Non-GDM women	GDM women	Non-GDM women	GDM women	Non-GDM women	GDM women		
Total sample								
Adjustment for age	1,067/18,856	327/1,142	163,703	6,503	1.00	7.02 (6.18-7.96)	<0.001	
Multivariate adjustment*	1,067/18,856	327/1,142	163,703	6,503	1.00	6.71 (5.91-7.63)	<0.001	
Age (y)*								<0.001
13.0-29.9	669/15,233	183/776	132,139	4,204	1.00	9.31 (7.87-11.0)	<0.001	
30.0-39.9	325/3,136	131/337	27,626	2,131	1.00	5.22 (4.24-6.42)	<0.001	
40.0-50.0	73/487	13/29	3,938	167	1.00	4.43 (2.43-8.09)	<0.001	
BMI (kg/m2)*								>0.50
<25.0	114/4,933	25/170	39,984	1,008	1.00	7.06 (4.51-11.1)	<0.001	
25.0-29.9	161/4,511	40/236	39,109	1,495	1.00	5.53 (3.86-7.91)	<0.001	
⩾30.0	792/9,412	262/736	84,610	4,000	1.00	6.76 (5.85-7.81)	<0.001	
Race*								>0.10
African American	733/12,484	206/638	112,511	3,758	1.00	7.41 (6.33-8.68)	<0.001	
White	300/5,145	89/337	43,954	2,036	1.00	5.23 (4.10-6.67)	<0.001	
Asian American	2/114	1/20	863	109	1.00	9.84 (0.39-249)	0.165	
Hispanic	13/452	14/71	2,826	293	1.00	9.92 (4.01-24.5)	<0.001	
Indian	8/101	4/13	939	64	1.00	6.09 (1.70-21.8)	0.005	
Race*‡								<0.025
African American	733/12,484	206/638	112,511	3,758	1.00	7.41 (6.33-8.68)	<0.001	
White	300/5,145	89/337	43,954	2,036	1.00	5.23 (4.10-6.67)	<0.001	

*GDM: gestational diabetes mellitus, BMI: body mass index.

†Adjusted for age, smoking, income, BMI, systolic blood pressure, race, other than the variable for stratification.

‡The analysis was restricted to African American women and white women, $\chi 2=5.51$, 1df, $p < 0.025$.

There was no significant interaction of BMI and a history of GDM on the risk of type 2 diabetes. However, there was a significant interaction between age and a history of GDM on risk of type 2 diabetes, which suggested that the extent of risk was stronger among women with gestational age 13.0-29.9 years than 30.0-50.0 years.

In race stratified analysis, White women tended to have the lowest risk to develop type 2 diabetes if they had a history of GDM (Table 8). Although there was no overall significant interaction between race and a history of GDM on the risk of type 2 diabetes, the risk was significantly different between African American women and White women (χ^2=5.51, df=1, p <0.025), suggesting that the relative risk for developing type 2 diabetes was higher in African American women with a history of GDM than in White women with a history of GDM (Table 8).

The incident rate of type 2 diabetes was declined over years during the postpartum period in both GDM and non-GDM women (Table 9), however, GDM women had higher incident rate at any given years compared to non-GDM women. Also, compared with non-GDM women compartments, GDM women after delivery for <1, 1.0-3.9, 4.0-5.9 , 6.0-7.9, 8-9.9, and ≥10.0 years had 5.31 (95% CI 3.43-8.23), 6.86 (CI 5.14-9.14), 4.92 (CI 3.27-7.39), 3.41 (CI 2.17-5.36), 4.81 (CI 3.06-7.57), and 3.54 (2.24-5.58) times higher risk of having type 2 diabetes, respectively.

Discussion

The present study involved 62,685 pregnancies, among which 19,998 were free of type 2 diabetes at baseline. This study constitutes the first investigation of the GDM incidence and the influence of a history of GDM on subsequent type 2 diabetes in Louisiana. This study suggested that, among women who received medical care from the LSUHCSD hospitals, the incidence of GDM increased in most years from 1997 to 2009 and reached a peak in 2002. The incidence of GDM was highest among women at 35.0-39.9 years of age, as

well as in Asian Americans. This study also suggested a direct association between a history of GDM and the risk of type 2 diabetes. African American women with a history of GDM showed a higher relative risk for incident type 2 diabetes than White women with a history of GDM. In addition, risk of type 2 diabetes was decreased by the time after index delivery.

In the present study, the age-standardized incidence of GDM increased from 5.8% in 1997 to 7.5% in 2009 (increased by 29.3%), suggesting an increase in GDM incidence in Louisiana. According to the Department of Health and Hospitals of Louisiana, the population in Louisiana has a high prevalence of physical inactivity, overweight/obesity (Louisiana has the 4th highest rate of adult obesity (Lloyd, 2010)), diabetes, high blood cholesterol, high blood pressure, tobacco use, and poor nutrition (Hospitals., 2009). All these factors may contribute to the increasing incidence of GDM in Louisiana. Due to the differences in the diagnostic criteria used in defining GDM, variables included in analyses, the study period and the study population, it is difficult to compare our results to other studies.

Advanced age had been identified as an important risk factor of GDM by several studies.(Anna et al., 2008; Dabelea et al., 2005b; Ferrara et al., 2004; Getahun et al., 2008a; Zhang et al., 2011) While most of these studies found out that the prevalence/incidence of GDM increased with age, the study conducted by Zhang et al(Zhang et al., 2011) showed that the prevalence of GDM peaked in the 30-34 age group and declined in the group who aged over 35. Similarly, in the current study, the highest incidence of GDM was observed in the 35.0-39.9 age group instead of the 40.0-50.0 age group. Of note, the observations in both studies were based on much fewer pregnancies and GDM cases identified in the oldest age group compared with other age groups. This might explain the inconsistency between the two studies and other studies.

Like previous studies (Anna et al., 2008; Dabelea et al., 2005b; Ferrara et al., 2004), the present study found that the incidence of GDM was higher among Asian women than

Table 9. Odds ratio for type 2 diabetes according to different follow-up times after delivery*

	Participants, n		Incident DM case, n		Person-years		Incidence rate/1,000 person-years		Incidence rate ratio GDM/Non-GDM	Odds Ratio†	
	Non-GDM	GDM	Non-GDM	GDM	Non-GDM	GDM	Non-GDM	GDM		Non-GDM	GDM
GDM <1.0 y	538	149	108	77	505	96	213.9	802.1	3.75	1.00	5.31 (3.43-8.23)
GDM 1.0-3.9 y	3,131	366	202	119	10,033	965	20.1	123.3	6.13	1.00	6.86 (5.14-9.14)
GDM 4.0-5.9 y	2,553	158	174	44	14,537	826	12.0	53.3	4.44	1.00	4.92 (3.27-7.39)
GDM 6.0-7.9 y	3,020	166	171	29	23,174	1,215	7.4	23.9	3.23	1.00	3.41 (2.17-5.36)
GDM 8.0-9.9 y	3,477	135	158	32	33,575	1,235	4.7	25.9	5.51	1.00	4.81 (3.06-7.57)
GDM ≥10.0 y	6,137	168	254	26	81,879	2,166	3.1	12.0	3.87	1.00	3.54 (2.24-5.58)

*DM: diabetes mellitus, GDM: gestational diabetes mellitus.

†Adjusted for age, smoking, income, BMI, systolic blood pressure and race.

among White women and African American women. This race difference of GDM risk cannot be fully explained by the difference in age, family income, BMI, and smoking among races. A recent combined analysis of 7,414 Asian American and 140,291 non-Hispanic White adults indicated that Asian Indians, Chinese, and Filipinos were each more likely to develop diabetes than non-Hispanic Whites (Oza-Frank et al., 2009). It has been hypothesized that Asians have higher adiposity per unit BMI compared with other race/ethnic groups, leading to an increased risk of type 2 diabetes at lower BMI (WHO expert consultation, 2004). Besides adiposity, poor medical care, short stature and genetic factors may also contribute to the higher GDM incidence in Asian women.(Anastasiou et al., 1998; Chu et al., 2009; Groop and Orho-Melander, 2001; Jang et al., 1998) The difference of GDM rate between non-Hispanic Whites and African Americans is inconsistent in the literature. Several studies, including the current one,(Chu et al., 2009; Getahun et al., 2008a; Williams et al., 1999) found the GDM rate was lower in African Americans as compared with Whites, while others reported the opposite findings.(Dabelea et al., 2005b; Esakoff et al., 2005b; Rosenberg et al., 2005b) However, the reason for such discrepancy is unclear and certainly deserves further investigations.

Our results are consistent with previous studies and are in the same magnitude of the risk estimates: women with a history of GDM have an overall of 5.7-fold increased risk of type 2 diabetes compared with non-GDM women after the index pregnancy. Therefore, adequate emphasis should be attached to preventing type 2 diabetes in women with a history of GDM in Louisiana.

Although several studies assessing the association between a history of GDM and type 2 diabetes included mixed ethnic origin subjects (Feig et al., 2008; Gunderson et al., 2007; Lee et al., 2007; Vambergue et al., 2008), no previous study has compared the relative risk of developing future type 2 diabetes between African American women and White

women with a history of GDM. In the current study, African American women with a history of GDM were more prone to developing subsequent type 2 diabetes than White women with a history of GDM, which may partly explain the much higher prevalence of diabetes in African American women than that of White women (Cowie et al., 2009) even though the rate of GDM is a little lower in African American women than in White women (Getahun et al., 2008b). This is also supported by our data which indicated that the incident rate of type 2 diabetes was similar in African American and White women who did not have a history of GDM.

In the current study, parous women with a history of GDM had a marked risk of progressing to diabetes: 802.1 incident rate per 1000 person-years over the subsequent year, and 53.3-123.3 incident rate per 1000 person-years over the following 1-5 years, which is in line with the finding from others that the cumulative incidence of type 2 diabetes increased markedly in the first 5 years postpartum (Kim et al., 2002). However, there is no sign of plateau after 10 years (12.0 incident rate per 1000 person-years). This may be partly explained by different duration of follow-up, different definition of cohort, ethnic variation as well as difference in diagnosis criteria of GDM and type 2 diabetes. Nevertheless, our results provide important data to suggest the cost-effectiveness interventions among women with a history of GDM may need to be introduced as early as possible postpartum.

SUMMARY AND CONCLUSION

In the current study, in women served by the LSUHCSD hospitals, the incidence of GDM increased in most years from 1997 to 2009 (from 5.8% to 7.5%) and reached a peak in 2002 (8.3%). GDM has become an important public health problem, particularly among women aged 35.0-39.9 years. Furthermore, in this cohort, a history of GDM is a strong predictor of incident type 2 diabetes later in life. African American women with a history of GDM showed a higher relative risk for incident type 2 diabetes than White women with a history of GDM. Therefore, more effort should be put into planning and implementation of effective prevention and control strategies for GDM in Louisiana especially in the middle and low income women. A lifestyle intervention targeting women, especially for African American women, with a history of GDM may be effective in reducing the burden of type 2 diabetes in Louisiana.

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APPENDIX: IRB FORM

Pennington Biomedical Research Center
LOUISIANA STATE UNIVERSITY SYSTEM

PBRC IRB FWA 00006218 ACTION ON PROTOCOL APPROVAL REQUEST

TO: **Gang Hu, Ph. D.**

FROM: Paula J. Geiselman, Ph.D., Chairman
PBRC Institutional Review Board for Research with Human Subjects

RE: IRB #PBRC 29035 **DATE:** November 19, 2010

Title: **Gestational Diabetes, Type 2 Diabetes, Cardiovascular Diseases and Death: The Relationship, the Course, and the Opportunity for Prevention.**

New Protocol/Modification: Continuing Review
Continuing Review Report 10/28/10; Study Summary; Protocol, No Informed Consent with this study – Limited Data Set.

Review Type: Full X **Expedited** ____ **Review Date:** November 17, 2010

Approved X **Disapproved** ____

Date of Approval: November 17, 2010 **Approval Expiration Date:** **November 16, 2011**
Re-review frequency: (annual unless otherwise stated) **Continuing Review report due:** 9/30/11
Number of subjects approved: N/A - Limited Data Set

By: Paula Geiselman, Ph. D., IRB Chair **Signature** ____

Continuing Approval is CONDITIONAL on:

1. Adherence to the approved protocol, familiarity with and adherence to the ethical standards of the Belmont Report and PBRC's Assurance of Compliance with DHHS regulations for the protection of human subjects.
2. Prior approval of a change in protocol, including an increased number of volunteers over that approved.
3. Obtaining renewed approval (or submittal of a termination report), prior to the approval expiration date, upon request by the IRB Office (regardless of when the project actually begins); notification of project termination.
4. Retention of documentation of informed consent and study records for at least 3 years after the study ends.
5. Continuing attention to the physical and psychological well-being and informed consent of the individual participants including notification of new information that might affect consent.
6. A prompt report to the IRB of any adverse event affecting a participant and potentially arising from the study.
7. Notification of the IRB of a serious compliance failure.

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VITA

Yujie Wang was born in Chongqing, People's Republic of China. She is the only daughter of Kaihua Wang and Minfeng Gao. Yujie received her Bachelor of Science Degree in Pharmacy in July 2003 from Chongqing Medical University, China. From 2003 to 2005, she worked in the Pharmacy Department of Chongqing Medical University as an Assistant Experimentalist. She was the only graduate selected to work in the department that year. In 2005, she was successfully admitted into a master program in pharmaceutics in Shanghai Jiao Tong University based on her excellent performance in the national entrance examination for master degree and her work experience. During her two-and-a-half year study, she participated in research projects, involving method development for the quality control of an important botanical drug under development. Yujie began a master's program in the spring of 2010 at Louisiana State University in the School of Human Ecology with a concentration in human nutrition and food. She is also a member of Phi Kappa Phi. After graduation, Yujie will continue working in nutritional epidemiology field.