

## **Evidence of a Relationship between Infant Birth Weight and Later Diabetes Mellitus and Impaired Glucose Regulation in a Chinese Population**

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## ABSTRACT

*Objective:* To determine the influence of birth weight, a marker of fetal growth, on the development of later impaired glucose metabolism throughout the life-span of people living in China.

*Research Design and Methods:* We recorded detailed anthropometric data including height, weight and health status and measured blood glucose levels and insulin concentrations at fast and 120 min of a standard OGTT from 2,019 eligible subjects born between 1921 and 1954 to investigate the risk of developing type 2 diabetes mellitus (DM) and impaired glucose regulation (IGR).

*Results:* The DM and IGR groups were characterized by significantly lower birth weight ( $P<0.001$ ), smaller head circumference ( $P<0.001$ ), smaller ponderal index (PI,  $P=0.007$ ), and shorter length ( $P=0.004$ ) in contrast to those in the normal glucose tolerance (NGT) group. Using multiple logistic regression analysis, we observed that birth weight remained significantly associated with DM and IGR after adjusting for possible confounding variables at birth and in adult life such as gender, age, central obesity, smoking status, alcohol consumption, dyslipidaemia, family history of diabetes and occupational status ( $p=0.027$ ). There was a significantly increased risk of getting DM and IGR for those with low birth weight (odds ratio 1.748 [95% confidence interval 1.018 to 3.001],  $p=0.043$ ).

*Conclusions:* The results confirm that lower birth weight is an independent risk factor for later diabetes or impaired glucose regulation, and show for the first time that this is also applies for a Chinese population.

**M**ost chronic non-communicable diseases originate as a result of the joint effects of genetic and environmental risk factors. Traditionally, risk factors associated with adult life style, such as smoking, diet and exercise habits, have attracted a great deal of interest. In more recent years, attention has also been paid to distal risk factors in early life. The intrauterine environment is now generally accepted as an important determinant of risk of disease in adulthood. The classic study by Barker and colleagues was the first to show that people with low birth weight had higher rates of type 2 diabetes later in life (1). Many studies have demonstrated an inverse relationship between body size at birth, as a marker of fetal growth, and diabetes mellitus or impaired glucose tolerance in adult life (2-10). However, many of these studies include only a few hundred individuals from developed countries (USA and Europe) (2-5). Few studies have been published exploring the relationship between intrauterine growth retardation (IUGR) and impaired glucose metabolism in later life in developing countries.

It is important to understand determinants of chronic diseases and health at later ages because populations in most countries are aging. China's population, in particular, is aging at an extraordinarily rapid pace. Chinese persons born 50-70 years ago have suffered frequent famine, civil wars, and invasions since the early 20th century. Nutritional impairment in *utero* due to poor nutrition of the mother, in concert with the development of energy dense and Westernized diet and life style in adults today, could lead to adverse health trends. To date, however, there have been few studies from developing

countries, including China, to test the fetal origins hypothesis. Thus, research on the relationship between IUGR and impaired glucose metabolism for Chinese people born 50-70 years ago is of particular significance.

We report the results of a follow-up study of people born in Peking Union Medical College Hospital (PUMCH) between 1921 and 1954. The study includes a quite large population of elderly and middle aged persons and extensive data on a wide range of dimensions at birth, gestational period and adult life. To test the fetal origin hypothesis, we paid particular attention to the interaction of early and later life factors.

## **RESEARCH DESIGN AND METHODS**

**Subjects.** The Peking Union Medical College Hospital in Beijing routinely keeps detailed obstetric records. Data include weight, length, head circumference at birth, placental weight, weeks of gestation, blood pressure at delivery and during the pregnancy, maternal parity, age, date of last menstrual period, etc. Authorities at the PUMCH allowed us to examine obstetric records of all 12,097 babies born at PUMCH from 1921 to 1954. We submitted their birth records identification data to the Beijing Population Registry Office and found 2,085 persons who were alive when the present study was conducted. The vast majority of them were living in the Beijing area. We recruited voluntary participants from these 2,085 persons. The Peking Union Medical College Ethical Committee approved the study and the study protocol was reviewed and approved by the NIH scientific review committee. All participants received informed consent.

We subsequently contacted the 2,019 participants who agreed to take part in the study and performed a follow-up during May 2003 and April 2005.

**Measurements.** A team consisting of trained and certified doctors, nurses, and technicians performed all measurements. An interview was conducted with each subject to determine history of chronic diseases and current health status using standardized procedures. Information on adult life status, including current occupation, smoking status, alcohol consumption, and family history of diabetes, was obtained through questionnaires. Height, weight, waist circumference, and blood pressure were also measured. The clinic staff was unaware of any obstetric information about the participants and their mothers. During the health examinations, blood samples were collected from the participants.

Participants attended the clinic after a 12-hour overnight fast. Then blood samples were drawn to measure plasma concentrations of glucose, insulin and serum levels of total cholesterol, high-density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglycerides (TG). Additional blood samples at 120 minutes after a standard (75g) oral glucose load were also taken to measure plasma levels of glucose and insulin. Oral glucose tolerance testing (OGTT 75g) was not performed in those persons who were already diagnosed as having diabetes.

Dyslipidaemia was defined as the presence of one or more of the followings: TG  $\geq 150$ mg/dl, total cholesterol  $\geq 220$ mg/dl, HDL-C  $\leq 40$ mg/dl, or LDL-C  $\geq 100$ mg/dl. Hypertension was defined as the presence of one or more of the followings: systolic blood pressure  $\geq 140$ mmHg, diastolic blood pressure

$\geq 90$ mmHg, or a definite history of hypertension with or without medicine. Diabetes was defined as the presence of one or more of the followings: fasting plasma glucose  $\geq 7.0$ mmol/l, glucose at 120 minutes  $\geq 11.1$ mmol/l, or a definite history of diabetes with or without medicine. The criteria (11) for impaired glucose regulation (IGR) were a fasting plasma glucose level of  $\geq 5.6$  to  $< 7.0$ mmol/l and/or a 2-h plasma glucose level at OGTT of  $\geq 7.8$  to  $< 11.1$ mmol/l. Central obesity was defined as waist circumference  $\geq 90$ cm for men and  $\geq 80$ cm for women, according to the International Diabetes Federation's (IDF) proposed definition of the metabolic syndrome in 2005 (12). Insulin resistance was determined by homeostasis model assessment (HOMA).  $HOMA-IR = \text{fasting plasma glucose (mmol/l)} \times \text{fasting plasma insulin (pmol/L)} / 22.5$  (13).

**Statistical Analysis.** Results are expressed as means  $\pm$  SD. Differences among groups were assessed by ANOVA for normally distributed continuous variables, by non-parametric tests (Kruskal–Wallis test) for non-normally distributed continuous variables (HOMA-IR, the number of pregnancies, parity), and by Chi-square tests for discrete variables. We analyzed the data derived from the birth records, clinic examinations and interviews, using multivariate logistic regression models, and controlling for possible confounding factors. In our logistic regression models, impaired glucose metabolism in adult life was the dependent variable, and mothers' status, measurements at birth, and adult status such as smoking status, alcohol consumption, and family history of diabetes, were the independent variables. Impaired glucose metabolism is defined as having either type 2 diabetes mellitus (DM) or impaired glucose regulation

(IGR). All statistics were run on SPSS 12.0 for Windows.

## RESULTS

Among a total of 2,019 subjects, 1,064 revealed a normal glucose tolerance (NGT), while 391 and 564 individuals were found to exhibit type 2 diabetes mellitus (DM 19.4%) and impaired glucose regulation (IGR 27.9%) respectively. Of those, 54 were already known to have type 2 diabetes mellitus and received anti-diabetes treatment prior to the present study.

Table 1 describes the baseline characteristics of the study subjects and the statistical test of the differences between the DM, IGR, and NGT groups, not adjusted for confounding factors. There were no significant gender differences among the three groups of DM, IGR, and NGT (not shown). However, there were significant age differences ( $P < 0.001$ ). The mean gestational weeks, parity and placental weight, and the number of pregnancies were similar in all three groups. There were large differences related to birth weight, length, head circumference and ponderal index (PI) among the three groups. The DM and IGR groups were associated with significantly lower birth weight ( $P < 0.001$ ), smaller head circumference ( $P < 0.001$ ), smaller PI ( $P < 0.001$ ), and shorter length ( $P = 0.004$ ) in contrast to the NGT group.

The association between maternal and neonatal characteristics and diabetes and impaired glucose regulation, without controlling for confounding factors, is shown in table 2. There is a powerful association between low birth weight, small length, head circumference and PI, and DM and IGR (collectively referred to below as impaired glucose metabolism). While an inverse association between

impaired glucose metabolism and four categories of birth weight and head circumference, and five categories of PI was evident. No systematic effect was apparent regarding placental weight and gestational weeks.

In tables 3 and 4, DM and IGR were combined as impaired glucose metabolism in the logistic regression analysis. After simultaneous adjustment for the perinatal confounding factors, as shown in the final column of table 3, the significant association was identified only between birth weight and impaired glucose metabolism exclusively ( $P < 0.001$ ). The risk of impaired glucose metabolism in those with low birth weight ( $< 2500\text{g}$ ) was nearly 2 times higher than those with normal birth weight. The effect of head circumference and PI on impaired glucose metabolism was much attenuated and no longer significant ( $P > 0.05$ ).

Table 4 shows the strength of the association between impaired glucose metabolism and birth weight, controlling for possible confounding factors both at birth and in adulthood.

The present study showed that impaired glucose metabolism was significantly associated with facets of adult life status such as age, smoking, being overweight, family history of diabetes, hypertension and dyslipidaemia (results not shown). Furthermore, adjustment for possible confounding factors at birth and in adult life, such as gender, age, central obesity, smoking status, alcohol intake, hypertension, dyslipidaemia, family history of diabetes and occupational status, led to only a small reduction in the strength of the association between birth weight and impaired glucose metabolism (table 4,  $p = 0.027$ ). Lower birth weight is an independent risk factors for impaired

glucose metabolism in adult life (OR 1.748, [95% confidence interval 1.018 to 3.001],  $p=0.043$ ).

## **CONCLUSIONS**

In this retrospective study, we explored the prevalence of impaired glucose regulation and diabetes in a quite large birth cohort of Chinese born in PUMCH between 1921 and 1954. There was little difference between males and females in the frequency of DM and IGR in this population. The prevalence of IGR (27.9%) and diabetes (19.4%) is consistent with other survey data from populations with a comparable age span (14). Our data broadly confirm previous studies showing that low birth weight is associated with a higher prevalence of impaired glucose metabolism (2-10,15-17), while our investigation is based on a substantially larger sample of middle-age and elderly subjects than that of previous studies.

A crucial critique of the previous clinical studies that support the fetal origins hypothesis is that they have not adequately unadjusted for confounding factors, such as smoking, alcohol consumption, diet, life style, social class, etc (20). In comparison with many other published studies, we had access to data containing more elaborate measures at birth and in adult life. Our data on confounding factors, at birth and in adult life, cover many different dimensions of socioeconomic status. We found a small attenuation of the effect of birth weight after adjusting for confounding factors at birth and in adult life, thus confirming that the effect of birth weight on glucose tolerance was independent of various other confounding factors. It should be acknowledged that, due to the retrospective nature of the present study, we could not collect information on

parental obesity and glucose intolerance, which may affect the glucose metabolism of their offspring and complicate modeling. A future prospective study on this very important issue is highly warranted.

In summary, these data provide the most compelling evidence to date that there is a genuine association between size at birth and risk of impaired glucose homeostasis in Chinese people, after adjusting for various confounding factors in adulthood. Based on present findings, we tentatively conclude that partially established fetal under-nutrition may be a risk factor for impaired glucose tolerance or frank type 2 diabetes in adulthood. This risk is independent of those associated with adult obesity, age, smoking, alcohol consumption, and so on. In developing countries such as China, one may hypothesize that improved nutrition in girls and women may offer long-term benefits to their offspring. However, we also conclude that not only the environment of intrauterine development should be emphasized, but risk factors in adult life style and behavior should be highlighted, of which could be intervened on now. Interventions for all of these risk factors could lead to good health at old ages.

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## REFERENCES

1. Hales CN, Barker DJ, Clark PM, Cox LJ, Fall C, Osmond C, Winter PD: Fetal and infant growth and impaired glucose tolerance at age 64. *BMJ* 303: 1019-1022, 1991
2. Barker DJ, Hales CN, Fall CH, Osmond C, Phipps K, Clark PM: Type 2 (non-insulin-dependent) diabetes mellitus, hypertension and hyperlipidaemia (Syndrome X): relation to reduced fetal growth. *Diabetologia* 36: 62-67, 1993
3. Lithell HO, McKeigue PM, Berglund L, Mohsen R, Lithell UB, Leon DA: Relation of size at birth to non-insulin dependent diabetes and insulin concentrations in men aged 50–60 years. *BMJ* 312: 406-410, 1996
4. McCance DR, Pettitt DJ, Hanson RL, Jacobsson LT, Knowler WC, Bennett PH: Birth weight and non-insulin dependent diabetes: thrifty genotype, thrifty phenotype, or surviving small baby genotype? *BMJ* 308: 942-945, 1994
5. Curhan GC, Willett WC, Rimm EB, Stampfer MJ: Birth weight and adult hypertension and diabetes mellitus in US men. *Am J Hypertens* 9:11A, 1996
6. Pernille Poulsen, Allan Vaag: The Intrauterine Environment as Reflected by Birth Size and Twin and Zygosity Status Influences Insulin Action and Intracellular Glucose Metabolism in an Age- or Time-Dependent Manner. *Diabetes* 55: 1819-1825, 2006
7. Levy-Marchal C, Jaquet D: Long-term metabolic consequences of being born small for gestational age. *Pediatr Diabetes* 5: 147-153, 2004
8. Ravelli AC, Van Der Meulen JH, Michels RP, Osmond C, Barker DJ, Hales CN, Bleker OP: Glucose tolerance in adults after prenatal exposure to the Dutch famine. *Lancet* 351: 173-177, 1998
9. Singhal A, Fewtrell M, Cole TJ, Lucas A: Low nutrient intake and early growth for later insulin resistance in adolescents born preterm. *Lancet* 361: 1089-1097, 2003
10. Valdez R, Athens MA, Thompson GH, Bradshaw BS, Stern MP: Birth weight and adult health outcomes in a biethnic population in the USA. *Diabetologia* 37: 624-631, 1994.
11. Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care* 26 (Suppl 1): S5-20, 2003
12. International Diabetes Federation: The IDF consensus worldwide definition of the metabolic syndrome. Available from [http://www.idf.org/webdata/docs/Metabolic\\_syndrome\\_definition.pdf](http://www.idf.org/webdata/docs/Metabolic_syndrome_definition.pdf). Accessed 2 September 2005
13. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC: Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 28: 412-419, 1985
14. Harris MI, Hadden WC, Knowler WC, Bennett PH: Prevalence of diabetes and impaired glucose tolerance and plasma glucose levels in U.S. population aged 20-74 yr. *Diabetes* 36: 523-534, 1987
15. Hofman PL, Cutfield WS, Robinson EM, Bergman RN, Menon RK, Sperling MA, Gluckman PD: Insulin Resistance In Short Children With Intrauterine Growth Retardation. *J Clin Endocrinol Metab* 82: 402–406, 1997
16. Facchini FS, Hua N, Abbasi F, Reaven GM: Insulin Resistance as a Predictor of Age-Related Diseases. *J Clin Endocrinol Metab* 86: 3574–3578, 2001

17. Phillips DI, Goulden P, Syddall HE, Aihie Sayer A, Dennison EM, Martin H, Cooper C; Hertfordshire Cohort Study Group: Fetal and Infant Growth and Glucose Tolerance in the Hertfordshire Cohort Study: A Study of Men and Women Born Between 1931 and 1939. *Diabetes* 54 (Suppl.2):S145-S150, 2005
18. Ergaz Z, Avgil M, Ornoy A: Intrauterine growth restriction—etiology and consequences: What do we know about the human situation and experimental animal models? *Reproductive Toxicology* 20:301–322, 2005
19. Barker, DJ: In utero programming of chronic disease. *Clinical Science* 95:115–128, 1998
20. Kramer MS, Joseph KS: Enigma of fetal/infant-origins hypothesis. *Lancet* 348:1254-1255, 1996

**TABLE 1.** Means and ANOVA tests for baseline characteristics of the study subjects

Variable	DM (n=391)	IGR (n=564)	NGT (n=1064)	F/X2	P
<b>Measurements at birth</b>					
Birth weight (g)*	3015.62±469.01 (391)	3091.09±436.61 (558)	3153.88±459.09 (1055)	13.803	<0.001
Birth length (cm)	49.05±2.50 (388)	49.47±2.26 (560)	49.52±2.48 (1055)	5.488	0.004
Head circumference(cm) *	31.32±1.64 (390)	31.53±1.75 (555)	31.79±1.63 (1047)	12.057	<0.001
Ponderal index(kg/m <sup>3</sup> )	25.51±3.11 (388)	25.56±3.57 (557)	26.01±3.36 (1052)	4.939	0.007
Gestational weeks (WK)	39.05±2.10 (379)	39.21±1.99 (545)	39.25±2.14 (1037)	1.269	.81
Number of pregnancies†	3.08±2.37 (383)	2.78±2.05 (551)	2.78±2.12 (1042)	3.549	0.094
Placental weight ( g )	539.90±122.37 (363)	532.82±112.64 (525)	548.27±125.13 (980)	2.863	0.057
Parity†	2.80±2.11 (382)	2.50±1.84 (551)	2.49±1.83 (1042)	5.628	0.060
<b>Adult measurements</b>					
HOMA_IR†	3.84±4.24 (378)	2.39±2.03 (562)	1.49±1.08 (1056)	340.783	<0.001
Waist circumference	92.14±10.1 (367)	91.08±10.6 (539)	86.89±10.5 (1022)	47.956	<0.001
BMI(Kg/m <sup>2</sup> )	25.87±3.74 (373)	25.53±3.45 (550)	24.38±3.40 (1064)	34.864	<0.001
Age*	62.49±7.89 (384)	60.99±8.26 (564)	57.61±7.70 (1064)	67.842	<0.001

Ponderal index: Birth Weight / Length<sup>3</sup>. \*Significantly difference between DM and IGR, or between DM and NGT, or between IGR and NGT. † Kruskal Wallis Test. The statistical tests of the difference among the DM, IGR and NGT groups in this table are not adjusted for confounding factors.

**TABLE 2.**The association of neonatal characteristics with impaired glucose metabolism (Pearson Chi-Square tests)

Variable	DM(n=391)	IGR (n=564)	NGT(n=1064)	$\chi^2$	P
<b>Birth weight ( g )</b>				31.377	<0.001
<2500	29.2%(47)	26.1%(42)	44.7%(72)		
2500-3000	23.2%(146)	30.1%(189)	46.7%(293)		
3000-3500	16.2%(132)	27.7%(226)	56.1%(457)		
3500+	16.5%(66)	25.3%(101)	58.3%(233)		
<b>Ponderal index (kg/m<sup>3</sup>)</b>				18.616	0.017
<2.2	24.3%(34)	30.7%(43)	45.0%(63)		
2.2-2.4	23.1%(84)	30.9%(112)	46.0%(167)		
2.4-2.6	18.9%(119)	28.2%(177)	52.9%(332)		
2.6-2.8	15.7%(83)	26.5%(140)	57.8%(306)		
2.8+	20.2%(68)	25.2%(85)	54.6%(184)		
<b>Birth length(cm)</b>				14.456	0.071
<48	22.4%(94)	26.3%(110)	51.3%(215)		
48-49	21.0%(60)	25.9%(74)	53.1%(152)		
49-50	22.9%(83)	26.7%(97)	50.4%(183)		
50-51	17.2%(60)	31.5%(110)	51.3%(179)		
51+	15.5%(91)	28.8%(169)	55.6%(326)		
<b>Head circumference(cm)</b>				28.757	<0.001
<31	24.2%(133)	28.2%(155)	47.6%(262)		
31-33	18.7%(184)	29.9%(294)	51.4%(505)		
33+	15.9%(73)	23.1%(106)	61.0%(280)		
<b>Placental weight (g)</b>				8.799	0.368
<450	20.1%(67)	29.7%(99)	50.2%(167)		
450-525	21.2%(128)	27.9%(169)	50.9%(308)		
525-600	17.4%(81)	30.8%(143)	51.8%(241)		
600-675	17.4%(45)	24.4%(63)	58.1%(150)		
675+	20.3%(42)	24.6%(51)	55.1%(114)		
<b>Biparietal/ Birth length</b>				3.858	0.426
<0.18	16.5%(85)	28.9%(149)	54.6%(281)		
0.18-0.2	20.0%(249)	27.9%(347)	52.1%(647)		
0.2+	21.6%(50)	26.8%(62)	51.5%(119)		
<b>Gestational weeks</b>				6.947	0.139
Full term	18.8%(327)	28.0%(487)	53.2%(924)		
Premature birth	26.3%(36)	28.5%(39)	45.3%(62)		
Postterm pregnancy	18.6%(16)	22.1%(19)	59.3%(51)		

Note: The estimates of the association in this table are not adjusted for confounding factors.

**TABLE 3.** Logistic analyses of the relationship between peripartum characteristics and risk of impaired glucose metabolism in adulthood (odds ratio and 95% CI), adjusted for confounders at birth

Variable	OR	SE	95%CI	P
<b>SEX</b> (vs Male, n=876)				0.46
Female ( n=896 )	0.820	0.100	0.674~0.997	
<b>Birth weight ( g )</b> (vs 3000-3500 n=724)				<0.001
<2500(n=135)	1.985	0.232	1.260~3.129	0.003
2500-3000(n=552)	1.849	0.141	1.404~2.436	<0.001
3500+(n=361)	0.976	0.154	0.722~1.318	0.872
<b>Placental weight ( g )</b> (vs 525-600 n=440)				0.560
<450 (n=318)	0.833	0.161	0.608~ 1.143	0.258
450-525 (n=572)	0.915	0.132	0.706~1.186	0.503
600-675 (n=246)	0.785	0.167	0.566~1.088	0.146
675+ (n=196)	0.815	0.182	0.570~1.164	0.260
<b>Head circumference(cm)</b> (vs 31-33 n=878)				0.002
<31 (n=480)	1.141	0.127	0.889~1.464	0.300
>33 (n=414)	0.667	0.132	0.515~0.865	0.002
<b>Gestational hypertension</b> (vs No, n=1566)		0.154		0.473
Yes(n=206)	0.895		0.662~1.211	
<b>Maternal age(y)</b> (vs 21-35 n=1449)				0.792
<21 (n=156)	0.929	0.179	0.654~1.318	0.679
>35 (n=167)	1.102	0.184	0.769~1.579	0.598
<b>Parity</b> (vs 1, n=711)				0.116
2-3 (n=637)	1.106	0.117	0.880~1.391	0.387
4-5 (n=264)	1.121	0.156	0.826~1.521	0.465
>6 (n=160)	1.626	0.200	1.098~2.409	0.015

**TABLE 4.** Predictive factors for the presence of impaired glucose metabolism in adulthood (valid sample size n=1772), adjusted for confounders both at birth and in adulthood

Variable	OR	SE	95%CI	P
<b>AGE</b>	1.063	0.008	1.046~1.081	<0.001
<b>SEX</b> (vs Male , n=755)	0.938	0.151	0.698~1.261	0.671
<b>Birth weight ( g )</b> (vs 3000-3500, n=623)				0.027
<2500 (n=112)	1.748	0.276	1.018~3.001	0.043
2500-3000 (n=489)	1.625	0.166	1.174~2.249	0.003
3500+ (n=313)	1.006	0.183	0.703~1.440	0.973
<b>Placental weight ( g )</b> (vs 525-600, n=377)				0.666
<450 (n=275)	1.049	0.192	0.720~1.530	0.803
450-525 (n=500)	1.092	0.158	0.801~1.487	0.578
600-675 (n=217)	0.818	0.198	0.555~1.207	0.312
675+ (n=168)	0.894	0.217	0.584~1.368	0.605
<b>Maternal age(y)</b> (vs 21-35 n=256)				0.622
<21 (n=137)	0.814	0.212	0.537~1.232	0.330
>35 (n=144)	0.994	0.225	0.640~1.543	0.977
<b>Parity</b> (vs1, n=609)				0.288
2-3 (n=558)	0.917	0.142	0.695~1.211	0.542
4-5 (n=234)	0.828	0.188	0.573~2.1196	0.314
>6 (n=136)	1.327	0.250	0.813~2.167	0.257
<b>Gestational hypertension</b> (vs No n=1356)	0.891	0.183	0.622~1.277	0.530
<b>Triglyceride (mg/dl)</b> (Vs <150 n=941)	1.791	0.124	1.404~2.284	<0.001
<b>HDL cholesterol (mg/dl)</b> (vs>40, n=1382)	1.095	0.206	0.732~1.639	0.658
<b>LDL cholesterol (mg/dl)</b> (vs <100, n=183)	0.981	0.185	0.683~1.409	0.916
<b>Hypertension</b> (vs No, n=733)	1.860	0.121	1.468~2.356	<0.001
<b>Family history of diabetes</b> (vs No, n=1133)	2.149	0.133	1.656~2.789	<0.001
<b>Drinking</b> (vs No, n=1492)	2.225	0.341	1.140~4.345	0.019
<b>Central obesity</b> (vs No, n=545)	1.566	0.130	1.213~2.023	0.001
<b>Smoking status</b> (vs Never smoker, n=1108)				0.551
Current smoke (n=271)	0.961	0.182	0.673~1.374	0.829
Ex-smoker (n=158)	1.223	0.213	0.807~1.855	0.343
<b>Living alone</b> (vs No, n=655)	1.242	0.121	0.980~1.574	0.073
<b>Job(Current Social class)</b> (vs Physical labor, n=543)	1.083	0.236	0.682~1.719	0.578