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CLINICAL STUDY

# Birth weight and risk of type 2 diabetes, abdominal obesity and hypertension among Chinese adults

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## Abstract

*Objective*: To investigate the association between birth weight and risk of type 2 diabetes, abdominal obesity and hypertension among Chinese adults.

*Research methods and procedures*: Nine hundred and seventy-three individuals from a population-based cross-sectional survey for the prevalence of type 2 diabetes conducted in Shanghai in 2002 were enrolled and followed up to 2004 with yearly examination. Birth weight was classified into four categories: <2500, 2500–2999, 3000–3499 and ≥3500 g.

*Results*: In this study, there were 373 males and 600 females, with a mean age of 46.2±9.9 years. Fasting plasma glucose was higher in subjects with the lowest birth weight (<2500 g) compared with those with the highest birth weight. Waist circumference and systolic blood pressure showed U-shaped relationships with birth weight. Birth weight was found to be an independent risk factor for type 2 diabetes, abdominal obesity and hypertension. For type 2 diabetes, the crude odds ratio (95% confidence interval) was 3.17 (1.48–6.78) in the lowest birth weight category when compared with that in the highest birth weight category (≥3500 g) and the ratio increased to 3.97 (1.71–9.22) after adjustment for related variables. The highest prevalence of type 2 diabetes (34.5%) was observed among those with the lowest birth weight and abdominal obesity.

*Conclusions*: Birth weight is inversely associated with the risk of type 2 diabetes. Subjects with the lowest or the highest birth weight were associated with a high risk of developing abdominal obesity and hypertension. Low birth weight coupled with abdominal obesity is a strong predictor of type 2 diabetes.

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## Introduction

The fetal origins hypothesis proposes that type 2 diabetes, obesity, coronary heart disease and hypertension are initiated by undernutrition during sensitive periods of development, such as infancy and fetal life (1, 2). Low birth weight is considered to indicate undernutrition of the fetus in the uterus. Many epidemiological studies supported the hypothesis that those born with low birth weight were at an elevated risk of developing type 2 diabetes and other disorders during adulthood (3–12).

The association of birth weight with diabetes is well documented in various populations (3–7) and different ages (8–10). The prevalence of impaired glucose tolerance or type 2 diabetes inversely associated with birth weight was seen in children and adults (3, 13). Studies in Pima Indians and school children in Taiwan revealed a U-shaped relationship between birth weight and risk of type 2 diabetes (8, 9). In the reports of the Nurses' Health Study (10), a reversed J-shaped relationship was initially observed for the risk for developing type 2 diabetes. However, after adjustment for adult body mass index (BMI) and maternal history of diabetes, an inverse association within the whole range of birth weight became apparent.

Extensive epidemiological studies have demonstrated a linear relationship between birth weight and obesity in later life. Although some studies suggest that low birth weight might also be associated with increased abdominal fat accumulation (14), the majority of studies indicate that high birth weight is associated with increased BMI later in life (15, 16). Only a few studies found no association between birth weight and BMI (17).

To our knowledge, no previous study has reported the association between the birth weight and the risk of type 2 diabetes, obesity and hypertension among Chinese adults in an epidemiological study. The purpose of this study is to investigate this association based on the data


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from a sample of Chinese adults, derived from an epidemiological study for the prevalence of type 2 diabetes conducted in an urban community in Shanghai, China.

## Subjects and methods

### Subjects

In 2002, a cross-sectional survey for the prevalence of type 2 diabetes was conducted in an urban community in Shanghai, China. A stratified multistage cluster-sampling design was employed. First, four (Huoxin, Mingyuancun, Jinsheng, Jiangpu) out of 33 sectors were randomly sampled from the Pingliang community. Then, a sample of 2200 people was randomly selected from 18 000 eligible permanent inhabitants aged 15–74 years in the four sectors. Valid information was obtained from 2132 people of the sample, with a response rate of 96.9%. All subjects were interviewed with standardized questionnaires including information about physician-diagnosed diabetes and hypertension, family history of diabetes, maximum lifetime weight, educational background, lifestyle factors, such as cigarette smoking, alcohol consumption and presently used medications for hypertension and diabetes. Plasma glucose was measured during a 75 g oral glucose tolerance test (OGTT) and serum lipid profile assayed. These individuals were followed up to 2004 with yearly examination and evaluation, and the outcomes defined in 2004. This study was approved by the local ethics committee and informed consent was obtained from all participants. Among them, 1010 individuals (389 males and 621 females) were able to provide the complete information of their birth weight (18), which was taken from birth certification and hospital case records.

The birth weight was routinely measured in birth hospitals and the scales adjusted monthly in order to rule out bias.

In the present study, 973 individuals (373 males and 600 females) aged 18–74 years with the information on birth weight were enrolled. Four individuals with incomplete data and another 33 subjects below 18 years were not included in this study. Since only around half of the original sample was included in the present study, we compared the characteristics between those included and excluded. With the exception of age, no significant difference was found between the two groups on present weight, waist circumference, BMI, hip circumference, systolic blood pressure, diastolic blood pressure, high density lipoprotein (HDL) cholesterol, triglycerides, fasting plasma glucose and 2 h-postchallenge plasma glucose after adjustment for age and sex. One possible explanation regarding the difference of age is that most senior citizens had lost their birth certification.

### Measurements

Anthropometric measurements included; height, weight, waist circumference, BMI ($kg/m^2$), hip circumference and systolic/diastolic blood pressure. Body weight, height and waist circumference were respectively measured to the nearest 0.1 kg and 0.1 cm. Blood pressure was measured three times at the right arm with a conventional mercury sphygmomanometer after the subjects had rested for at least 5 min in the sitting position and the average of the last two measurements was used for analysis. All interviews were conducted by 20 well-trained medical workers. After 3 days, during which time the subjects were instructed to eat at least 150 g of carbohydrates per day, a standard 75 g OGTT was administered to them. The plasma glucose concentration was determined immediately after blood centrifugation by hexose-kinase method and serum lipid profile, by the enzymatic method. All measurements were made in the same laboratory.

### Definitions and categorical cut points

Birth weight was classified into four categories: $<$ 2500, 2500–2999, 3000–3499 and $\geq$3500 g. Type 2 diabetes was defined by a fasting plasma glucose level $\geq$7.0 mmol/l and/or a 2-h postchallenge glucose level $\geq$11.1 mmol/l, a previous diagnosis of type 2 diabetes, or using antidiabetic medication according to 1997 American Diabetes Association (ADA) Recommendations (19). Abdominal obesity was defined as waist circumference $\geq$90 cm for men and $\geq$80 cm for women (20). Hypertension was defined as an average measured systolic blood pressure $\geq$140 mmHg and/or diastolic blood pressure $\geq$90 mmHg, or the use of antihypertensive medication according to the guideline of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (21). Family history of diabetes was defined as at least one of the first-degree relatives or grandparents having diabetes. Five categories were set for the educational level: (i) no formal education, (ii) primary school, (iii) junior middle school, (iv) senior middle school and (v) college or university. Cigarette smoking was divided into: (i) never smoking, (ii) stopped smoking and (iii) smoking. For alcohol consumption, there were four groups: (i) never drinking, (ii) stopped drinking (iii) one time or less per month and (iv) twice per month or more.

### Statistical analysis

Descriptive data are shown as mean$\pm$S.D. Linear regression analyses with adjustment for age and sex were used to compare variables among the four birth weight categories and Fisher's least significant

difference *t*-tests were conducted in multiple comparisons. The association of birth weight with the related variables was tested by means of a quadratic term to account for non-linear association. Forward stepwise logistic regression models were used to find independent risk factors for type 2 diabetes, abdominal obesity and hypertension. To assess the association of birth weight and the risk of type 2 diabetes, abdominal obesity and hypertension, multivariate logistic regression analyses were applied in different models, and birth weights were entered as dummy variables. Odds ratios (ORs) with 95% confidence intervals (CI) were calculated to estimate the relative risk by birth weight category. Age, sex, waist circumference, family history of diabetes, educational background, cigarette smoking and alcohol consumption were covariates and adjusted in different models of analyses. All statistical analyses were performed using SPSS 11.0 (SPSS, Chicago, IL, USA). All statistical tests were two-tailed and $P$ value $\leq 0.05$ was considered statistically significantly different.

## Results

There were 373 males and 600 females in this study. The mean age of the sample was $46.2 \pm 9.9$ years ($45.2 \pm 10.6$ years for males and $46.9 \pm 9.5$ years for females). The mean values of anthropometric data and metabolic variables by birth weight category in 2004 were presented in Table 1. No significant difference was found in the distribution of age among the subjects by birth weight categories. Fasting plasma glucose was higher in subjects with the lowest birth weight ($<2500$ g) when compared with those with the highest birth weight (all at least $P<0.05$). Waist circumference, present weight, BMI and systolic blood pressure showed U-shaped relationships with birth weight ($P$ for quadratic terms $<0.05$). The results were similar in males and females (data not shown).

According to the ADA criteria, there were 114 (11.7%) individuals (50 males and 64 females) with type 2 diabetes. Birth weight, age (OR and 95% CI: 1.05, 1.03–1.08; $P=0.000$), waist circumference (OR and 95% CI: 1.06, 1.03–1.08; $P=0.000$) and family history of diabetes (OR and 95% CI: 2.09, 1.33–3.27; $P=0.001$) were found to be independent risk factors for type 2 diabetes in a forward stepwise logistic regression model.

ORs and 95% CI for type 2 diabetes by birth weight category, calculated using the highest birth weight ($\geq 3500$ g) as a reference (OR$=1$), are shown in Table 2. After adjustment for age, sex, waist circumference, family history of diabetes, educational background and cigarette smoking, alcohol consumption in different models, the inverse association between birth weight and the risk of type 2 diabetes emerged and became more obvious. The OR (95% CI) for type 2 diabetes, after adjustment for various related variables, was 3.97 (1.71–9.22) in the lowest birth weight category ($<$ 2500 g) when compared with that in the highest birth weight category ($\geq 3500$ g).

According to the aforementioned criteria, there were 359 (36.9%) individuals with abdominal obesity and 460 (47.3%) with hypertension. Birth weight, sex (OR and 95% CI: 1.89, 1.39–2.57; $P=0.000$), age (OR and 95% CI: 1.04, 1.03–1.06; $P=0.000$) and educational background (OR and 95% CI: 0.79, 0.66–0.94;

**Table 1** Mean value of anthropometric and metabolic variables by birth weight category among Chinese adults. Data are presented as mean ± S.D.

| | Birth weight category (g) | | | | | | |
|---|---|---|---|---|---|---|---|
| **Variables** | <2500 (*n*=55) | 2500–2999 (*n*=356) | 3000–3499 (*n*=405) | ≥3500 (*n*=157) | Total (*n*=973) | ***P*-value for linear model** | ***P*-value for quadratic terms** |
| Age (year) | 46.5±7.7 | 46.9±8.5 | 45.9±10.0 | 45.4±12.9 | 46.2±9.9 | 0.787 | – |
| Waist circumference (cm) | 81.9±10.4 | 77.6±8.3 | 76.4±9.3 | 83.3±10.6 | 79.5±9.4 | 0.000 | 0.000 |
| Current weight (kg) | 68.6±12.2 | 64.3±10.6 | 66.5±10.8 | 73.2±13.8 | 66.8±11.7 | 0.000 | 0.000 |
| Maximum lifetime weight (kg) | 68.2±11.7 | 66.2±11.0 | 68.5±11.8 | 75.5±12.6 | 68.8±12.0 | 0.002 | 0.000 |
| Height (cm) | 162.0±7.3 | 161.3±7.5 | 164.9±8.2 | 168.0±10.1 | 163.9±8.6 | 0.004 | 0.000 |
| Body mass index (BMI) ($kg/m^2$) | 26.1±3.9 | 24.6±3.4 | 24.4±3.3 | 25.7±4.0 | 24.8±3.5 | 0.000 | 0.019 |
| Systolic blood pressure (mmHg) | 130.7±19.9 | 124.1±17.7 | 124.8±16.9 | 129.6±17.2 | 125.7±17.5 | 0.001 | 0.035 |
| Diastolic blood pressure (mmHg) | 81.9±10.2 | 81.0±10.7 | 82.1±10.7 | 83.8±11.7 | 82.0±10.9 | 0.245 | – |
| Fasting plasma glucose (mmol/l) | 6.4±2.4 | 5.6±1.2 | 5.6±1.4 | 5.7±1.4 | 5.7±1.4 | 0.001 | – |
| Postchallenge plasma glucose (mmol/l) | 6.6±3.8 | 5.7±2.3 | 5.6±2.4 | 5.7±2.4 | 5.7±2.5 | 0.063 | – |
| HDL cholesterol (mmol/l) | 1.4±0.4 | 1.5±0.4 | 1.4±0.4 | 1.3±0.4 | 1.4±0.4 | 0.219 | – |
| Triglycerides (mmol/l) | 1.4±0.7 | 1.2±0.7 | 1.4±0.9 | 1.5±0.9 | 1.3±0.8 | 0.272 | – |

*P* value for generalized linear model with adjustment for age and sex was used to compare variables among birth weight categories and *P* value for quadratic terms was shown when birth weight and the related variables were tested by means of a quadratic term to account for non-linear associations.

**Table 2** Odds ratio (OR) for type 2 diabetes by birth weight category among Chinese adults.

| Variables | Birth weight category (g) | | | |
|---|---|---|---|---|
| | <2500 | 2500–2999 | 3000–3499 | ≥3500 |
| *N* (case/total) | 16/55 | 38/356 | 42/405 | 18/157 |
| Crude OR (95% CI) | 3.17 (1.48–6.78) | 0.92 (0.51–1.67) | 0.89 (0.50–1.61) | 1 |
| OR (95% CI) after adjustment for | | | | |
| Age | 3.49 (1.60–7.64) | 0.95 (0.52–1.75) | 0.94 (0.52–1.71) | 1 |
| Age and sex | 3.93 (1.77–8.74) | 1.11 (0.59–2.09) | 1.00 (0.55–1.84) | 1 |
| Age, sex and waist circumference | 3.93 (1.74–8.89) | 1.37 (0.71–2.62) | 1.19 (0.64–2.21) | 1 |
| Age, sex, waist circumference and family history of diabetes | 3.83 (1.66–8.84) | 1.34 (0.70–2.59) | 1.20 (0.64–2.24) | 1 |
| Age, sex, waist circumference, family history of diabetes and educational background | 3.87 (1.68–8.92) | 1.33 (0.69–2.57) | 1.21 (0.65–2.27) | 1 |
| Age, sex, waist circumference, family history of diabetes, educational background, cigarette smoking and alcohol consumption | 3.97 (1.71–9.22) | 1.35 (0.70–2.61) | 1.24 (0.65–2.33) | 1 |

CI, confidence interval.

$P=0.009$) were independent risk factors for abdominal obesity, while those for hypertension were birth weight ($P=0.001$), age (OR and 95% CI: 1.08, 1.06–1.10; $P=0.000$), family history of diabetes (OR and 95% CI: 1.43, 1.03–1.96; $P=0.031$) and height (OR and 95% CI: 1.02, 1.00–1.04; $P=0.023$) in the forward stepwise logistic regression models.

Results from multivariate logistic regression analyses to estimate the relative risks for abdominal obesity and hypertension by birth weight category in different models were shown in Tables 3 and 4. In the multivariate logistic regression models, ORs and 95% CI were calculated by birth weight category using birth weights in the range 2500–2999 g for reference (OR$=$1). Using the reference group, all OR values were more than 1, which is convenient to read. The ORs for obesity and hypertension for subjects with both the lowest and the highest birth weights were higher than those for subjects with the birth weight category of 2500–3499 g.

Moreover, we adopted stratified analyses by dividing all subjects into two categories (abdominal obesity and non-obesity) according to adult waist circumference. The prevalence of type 2 diabetes in abdominally obese adults was remarkably higher than that in non-obese individuals. From Figure 1 we can see that the highest rate of type 2 diabetes (34.5%) was observed in the lowest birth weight category (<2500 g) among adults with abdominal obesity. Another conclusion was that waist circumference had a strong impact on diabetes risk in the highest birth weight group, which showed a threefold increase in risk.

**Table 3** Odds ratio (OR) for abdominal obesity by birth weight category among Chinese adults.

| Variables | Birth weight category (g) | | | |
|---|---|---|---|---|
| | <2500 | 2500–2999 | 3000–3499 | ≥3500 |
| *n* (case/total) | 29/55 | 127/356 | 137/405 | 66/157 |
| Crude OR (95% CI) | 2.01 (1.14–3.56) | 1 | 0.92 (0.68–1.24) | 1.31 (0.89–1.92) |
| OR (95% CI) after adjustment for | | | | |
| Age, sex, educational background, cigarette smoking and alcohol consumption | 2.26 (1.25–4.08) | 1 | 1.12 (0.81–1.53) | 1.88 (1.23–2.88) |

**Table 4** Odds ratio (OR) for hypertension by birth weight category among Chinese adults.

| Variables | Birth weight category (g) | | | |
|---|---|---|---|---|
| | <2500 | 2500–2999 | 3000–3499 | ≥3500 |
| *n* (case/total) | 32/55 | 146/356 | 191/405 | 91/157 |
| Crude OR (95% CI) | 2.00 (1.13–3.56) | 1 | 1.28 (0.96–1.71) | 1.98 (1.36–2.90) |
| OR (95% CI) after adjustment for | | | | |
| Age, sex, educational background, cigarette smoking and alcohol consumption | 2.07 (1.13–3.78) | 1 | 1.29 (0.95–1.76) | 2.09 (1.36–3.20) |

CI, confidence interval.

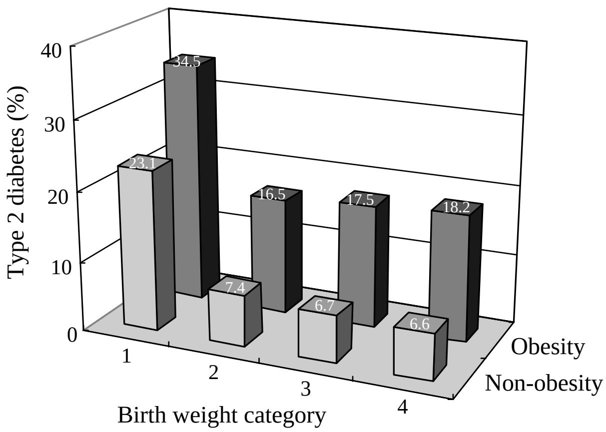


**Figure 1** The effect of birth weight and abdominal obesity on the prevalence of type 2 diabetes among Chinese adults

## Discussion

With the rapid increase of economy and the transition of life style, the prevalence of type 2 diabetes and obesity is rising dramatically in China (22, 23). Type 2 diabetes and obesity are known risk factors for increased cardiovascular diseases and it has been suggested that it is critical to decrease the incidence of diabetes and obesity for the prevention of cardiovascular diseases. In recent years, one method has emerged from the notion that environmental factors in infancy and fetal life can have a profound influence on lifelong health.

In the present study, we analyzed the association between birth weight and the risk of type 2 diabetes, abdominal obesity and hypertension among Chinese adults.

The association between birth weight and the risk of type 2 diabetes was confirmed by the results of our study. Fasting plasma glucose was higher in subjects with the lowest birth weight ($<2500$ g) compared with those with the highest birth weight. Birth weight was an independent risk factor for type 2 diabetes. In Particular, birth weight was inversely associated with the risk of type 2 diabetes, and the risk was about four times higher among those with the lowest birth weight ($<2500$ g) as compared with those with the highest birth weight ($\geq 3500$ g), after adjustment for a number of related variables. These findings are in agreement with the results of many previous reports (3, 10, 13). However, the fact that low birth weight is linked to type 2 diabetes by way of insulin resistance and/or insulin deficiency is highly controversial. More recent findings have indicated that insulin resistance (4, 24–26) and subclinical inflammation may explain the increased risk of type 2 diabetes. In the MIDSPAN family study, part of the association of low birth weight with elevated risks for type 2 diabetes in later life could be mediated by the inflammatory pathway (27).

In the present study, we found that weight, waist circumference and BMI showed U-shaped relationships with birth weight ($P$ for quadratic terms $<0.05$). Moreover, birth weight is an independent risk factor for abdominal obesity in adulthood. The U-shaped relationships were observed for the risk of developing abdominal obesity across four birth weight categories. Subjects with the lowest and the highest birth weights were linked to the risks of developing abdominal obesity, compared with those in the birth weight category of 2500–3499 g.

Though an association between birth weight and abdominal obesity during adulthood among Chinese adults was found in our study, the mechanism that could explain the relationships has not yet been clarified. It is well known that obesity is an important risk factor for type 2 diabetes. However, a significant difference across different birth weight categories was found in the prevalence of type 2 diabetes in our study. In the obese subjects born with the highest birth weight, the incidence of type 2 diabetes was lower (18.2%) than in those born with the lowest birth weight (34.5%), indicating a possibility of different pathogenesis of obesity in subjects with low and high birth weights. Recent studies showing that high birth weight is associated with increased height and lean body mass, but not with increased adiposity later in life in Pima Indians (28) support our findings. Therefore, more evidence about increased cardiovascular risk across different birth weight categories remains to be investigated in the future.

Obesity in adults is a known risk factor for many metabolic diseases and its role in the risk of type 2 diabetes was analyzed together with birth weight in the present study. Recent findings indicate that waist circumference is a stronger marker of health risks than BMI (29). Since, ethnic differences are likely to exist between populations, we adopted the criteria of waist circumference of 90 cm in men and 80 cm in women as the cut-off for the definition of abdominal obesity among Chinese adults. In our study, the prevalence of type 2 diabetes in abdominally obese adults was remarkably higher than that in non-obese individuals. For example, waist circumference had a strong impact on diabetes risk in the highest birth weight group, which showed a threefold increase in risk. In Particular, subjects with the lowest birth weight and adult obesity had the highest prevalence of type 2 diabetes (34.5%). Therefore, for the prevention of type 2 diabetes, strong measures aimed at decreasing waist circumference should be taken in subjects both with low and high birth weights. The fact that present abdominal obesity may have great effect on the prevalence of type 2 diabetes in adult obesity subjects in our study is not surprising, because abdominal obesity is known to be a major factor in determining subclinical inflammation and insulin resistance.

It has been shown in many studies that birth weight is negatively associated with systolic blood pressure after controlling possible variables (30, 31). However,

Tu *et al.* indicated that the association is due to the inappropriate adjustment for variables such as present weight (32). In our study, birth weight is an independent risk factor for hypertension. In addition, systolic blood pressure showed U-shaped relationships with birth weight (*P* for quadratic terms $<0.05$). Both the lowest and the highest birth weights have been linked to the risk of developing hypertension among Chinese adults.

One limitation of the present study is that birth weight was provided by only half of the epidemiological study population. Nevertheless, anthropometric data and metabolic variables analysis showed that, with the exception of age, there were no significant differences between those included and excluded. Hence, the results from the present study could be considered to have reflected the situation among urban Chinese adults in general.

In summary, an inverse association between birth weight and the risk of type 2 diabetes, and U-shaped relationships between birth weight and abdominal obesity and hypertension were found in our study, after adjustment for a number of related variables. Birth weight is an independent risk factor for abdominal obesity and hypertension. Birth weight and abdominal obesity were independent risk factors for type 2 diabetes. Therefore, for prevention of type 2 diabetes, more measures should be taken to decrease the prevalence of lower birth weight infants. On the other hand, keeping an appropriate waist circumference in lifetime is important for one's health.

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