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Associations of maternal cyclin-dependent kinase 5 regulatory subunit-associated protein 1-like 1(*CDKAL1)* gene variants with adverse pregnancy outcome in Chinese women

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Abstract

Objective To test associations of cyclin-dependent kinase 5 regulatory subunit-associated protein 1-like 1 (*CDKAL1*) gene variants with the risk of adverse pregnancy outcome in Chinese women and whether the association was mediated by occurrence of gestational diabetes mellitus.

Methods We organized a 1:1 age-matched study nested within a prospective cohort of pregnant women (207 pairs) established in urban Tianjin. Adverse pregnancy outcome was defined as a composite outcome of preterm birth, low birth weight or macrosomia. Logistic regression analyses were used to estimate associations of *CDKAL1* gene variants with adverse pregnancy outcome and its components. The *CDKAL1* genetic marker was defined as encompassing any of the identified susceptibility variants for adverse pregnancy outcome.

Results The *CDKAL1* genetic marker was associated with the risk of adverse pregnancy outcome (OR: 2.51, 95%CI: 1.47, 4.28), low birth weight (OR: 19.80, 95%CI: 2.15, 182) and macrosomia (OR: 2.40, 95%CI: 1.17, 4.93), but not with preterm birth ($P=0.105$) after adjusting for traditional risk factors. Further adjusting for gestational diabetes mellitus, the *CDKAL1* genetic marker remained significantly associated with adverse pregnancy outcome, and the OR (95%CI) was 2.52 (1.48, 4.30).

Conclusion The maternal *CDKAL1* gene variants were associated with increased risk of adverse pregnancy outcome, low birth weight and macrosomia, independent of gestational diabetes mellitus. *CDKAL1* gene might be a useful marker for identification of individuals at a particularly high risk of adverse pregnancy outcome in early pregnancy.

Keywords *CDKAL1* gene, Adverse pregnancy outcome, Gestational diabetes mellitus, Low birth weight, Macrosomia

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Introduction

The cyclin-dependent kinase 5 regulatory subunit-associated protein 1-like 1 (*CDKAL1)* gene was associated with reduced pancreatic β-cell function, which affected insulin secretion in response to changes in plasma glucose levels [1]. It was confirmed in different populations, such as Koreans and Russians, that specific genetic variants of *CDKAL1* increased susceptibility to type 2 diabetes (T2D) and gestational diabetes mellitus (GDM) [2, 3]. Our study further verified that the *CDKAL1* rs7747752 increased the risk of GDM in Chinese women [4]. It was well-known that GDM increased the risk of adverse pregnancy outcomes, including shoulder dystocia, cesarean section, macrosomia, hypocalcemia, preterm birth, low birth weight, and others [5–8]. Additionally, GDM elevated the risk of developing diabetes in the mother later in life and increased the risk of obesity in the offspring [9–11]. Several studies explored the association between fetal *CDKAL1* genotype (rather than maternal genotype) and their birth weight, but the conclusions were inconsistent [12, 13]. However, no studies have focused on whether maternal *CDKAL1* genetic variants increased the risk of adverse pregnancy outcomes. Therefore, it is essential to explore whether the maternal *CDKAL1* gene variants increased the risk of adverse pregnancy outcomes and whether this process was mediated through GDM.

Our study aimed to test the association of maternal *CDKAL1* gene variants with the risk of adverse pregnancy outcome (APO), including any of preterm birth, low birth weight, or macrosomia, and whether it was mediated by GDM, based on a previous nested case–control study in a prospective cohort of pregnant women with GDM in Tianjin, China [14].

Method

Research design and participants

The design and population of the study have been described previously [14]. We established a prospective cohort of 22,302 pregnant women from 6 urban districts of Tianjin, China from October 2010 to August 2012. This research protocol was approved by the Clinical Research Ethics Committee of Tianjin Women's and Children's Health Center (TWCHC). Written informed consent was obtained from the participants before data collection. This study was performed in line with the principles of the Declaration of Helsinki.

A tiered screening strategy was employed to identify cases of GDM. Initially, at primary healthcare institutions, all participants were invited to complete a 1-h 50-g oral glucose challenge test (GCT) at 24–28 weeks of gestation. Participants exhibiting GCT results ≥ 7.8 mmol/L were subsequently referred to a dedicated GDM clinic within TWCHC for a more comprehensive assessment. At this stage, they underwent a 2-h 75-g oral glucose tolerance test (OGTT) after more than 8 h of fasting. The diagnostic criteria for GDM adhered to the International Association of Diabetes and Pregnancy Study Groups (IADPSG), which encompassed a fasting plasma glucose (PG) ≥ 5.1 mmol/L, a 1-h PG ≥ 10.0 mmol/L, or a 2-h PG ≥ 8.5 mmol/L [15].

In this cohort, 2,991 women out of 22,302 pregnant donated their blood samples during early pregnancy at the early stage of the study. Among the remaining 2,764 participants with OGTT results available, 243 women with GDM were used as the study cases and 243 healthy women with matched maternal ages (± 1 y) were selected as the controls. Among the 486 women, 16 women with low capacity of DNA extraction, 23 women who lacked high-quality DNA data and 33 women who did not have an age-matched GDM counterpart or control were excluded. The remaining 207 pairs of GDM patients and controls ($n = 414$) were eligible for this study (Fig. 1).

Data collection procedure

We collected pregnancy information on height, weight, maternal age, systolic/diastolic blood pressure (BP), parity, ethnicity, family history of diabetes in first-degree relatives, education level, and gestational age at registration. Besides we collected delivery information including infant gender, birth weight of neonates, body height of neonates, and delivery week. Pre-pregnancy body mass index (BMI) (kg/m^2) was estimated as pre-pregnancy weight (kg) divided by height squared (m^2). Hypertension was defined as systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg [16].

Ascertainment of APO

APO was defined as any of preterm birth, low birth weight, or macrosomia in our study. Preterm birth was defined as delivery week < 37 weeks [17]. Low birth weight was identified as birth weight of neonates < 2,500 g and macrosomia referred to ≥ 4,000 g [18].

Genotyping

Blood samples were collected in the fasting state at registration and stored at − 80℃ until use. DNA samples were genotyped by the Illumina Infinium® Global Screening Array. The genotype data were imputed using minimac 3 with the 1000 Genomes Project phase 3V5 as a reference panel. Based on the single nucleotide polymorphism (SNP) database, the following quality control steps were implemented: (1) Samples with a call rate < 97% were filtered out; (2) SNPs with > 20% missing data and individuals with > 2% missing genotype data were removed; (3) Subjects with discrepant gender information were excluded; (4) Individuals with a minor allele frequency < 1% were filtered out; (5) SNPs

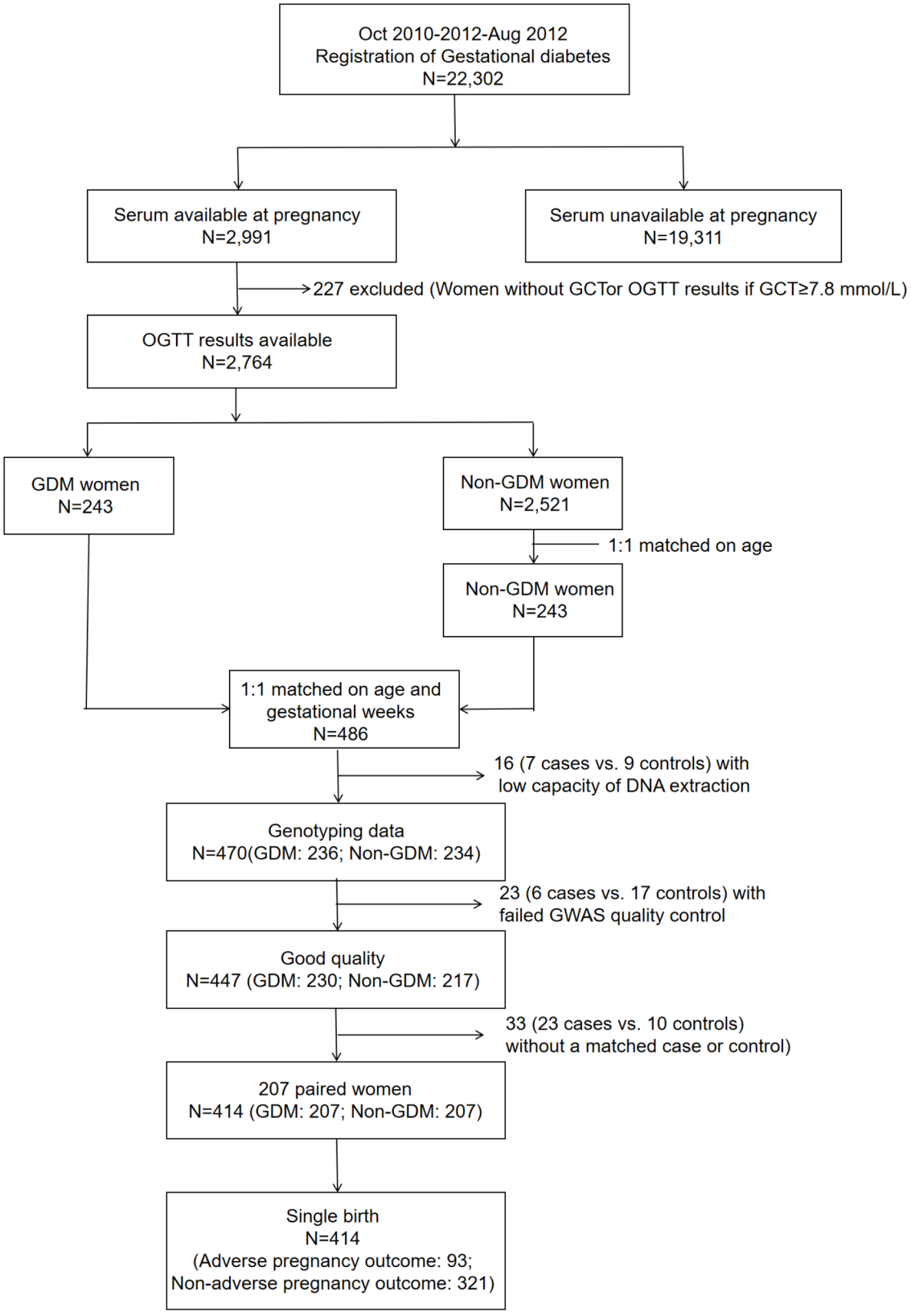

Fig. 1 Title: Patient flowchart
Legends: Adverse pregnancy outcome included any of preterm birth, low birth weight, or macrosomia
Abbreviations: GCT, glucose challenge test; OGTT, oral-glucose-tolerance test; GDM, gestational diabetes mellitus; DNA, Deoxyribonucleic Acid; GWAS, genome-wide association study

with a Hardy-Weinberg equilibrium P-value $< 1 \times 10^{-4}$ were filtered out; (6) Individuals deviating from the mean heterozygosity rate by ± 3 standard deviations (SD) were excluded; (7) Relatedness and ancestry outliers (pi-hat > 0.2, concordance > 0.98) were identified and filtered out [19]. Genotyping data from specific candidate SNP (*CDKAL1* gene variants) were extracted from the genome-wide genotyping. The overall genotype call rate was 99.4%.

Statistical analysis

Continuous data were presented as mean ± SD or median [interquartile range, (IQR)] and compared by t-test or Wilcoxon rank sum test, while categorical variables were presented by number (percentage) and compared by chi-square tests or Fisher's exact test. Firstly, logistic regression analyses were used to estimate the odds ratios (ORs) and corresponding 95% confidence intervals (95%CIs) of *CDKAL1* gene variants on the risk of APO and its components, including preterm birth, low birth weight, and macrosomia. The *CDKAL1* genetic marker was defined as encompassing any one of identified susceptibility variants related to APO, and accordingly, ORs and their corresponding 95%CIs for the risk of APO and its components were calculated using logistic regression analyses.

To control for potential confounding factors associated with APO, traditional risk factors, including age, pre-pregnancy BMI, family history of diabetes in first degree relatives, parity, education, Han ethnicity, hypertension, infant gender, and body height of neonates, were adjusted in the adjusted model 1. Further adjusted for GDM in the adjusted model 2 to explore the mediation effects of GDM on the association of *CDKAL1* genetic marker and APO.

Analysis was performed using R (R Core Team, 2024. R Foundation for Statistical Computing, Vienna, Austria.). A P value < 0.05 was considered to be statistically significant.

Results

Characteristics of the participants with APO

For the 414 pregnant women included in this study, the median age was 29 years and the median gestational age was 10 weeks at registration. There were 93 women who experienced an APO among the included participants. Compared to women without APO, women with APO had a higher pre-pregnancy BMI and a lower value of delivery week. Women with APO were more likely to have genotypes AG/AA for *CDKAL1* rs141859146 and CT/CC for rs7762612. And the remaining 21 maternal *CDKAL1* gene variants had no statistical differences in the women with and without APO group (Table 1 and Appendix Table 1).

Associations of maternal *CDKAL1* gene variants on the risk of APO

In the dominant model, maternal *CDKAL1* rs141859146 (AG/AA vs. GG), rs7762612 (CT/CC vs. TT) and rs4710944 (TC/TT vs. CC) were associated with the risk of APO in the univariate analyses, with the ORs (95%CIs) were 3.62 (1.14, 11.5), 2.04 (1.18, 3.54), and 2.82 (1.02, 7.80) respectively (Table 2). Other remaining 20 maternal *CDKAL1* gene variants were not associated with the risk of APO (Appendix Table 2).

Maternal *CDKAL1* genetic marker on APO and its components

CDKAL1 genetic marker was defined as encompassing any of the susceptibility variants rs141859146, rs7762612 or rs4710944 for APO. Compared to women without *CDKAL1* genetic marker, women with *CDKAL1* genetic marker were more likely to have APO and had higher birth weight and height of neonates. There were no statistical differences in other characteristics, such as maternal age and pre-pregnancy BMI, etc., between the groups with and without the *CDKAL1* genetic marker (Appendix Table 3).

Maternal *CDKAL1* genetic marker was significantly associated with the risk of APO, with the OR (95%CI) was 2.34 (1.41, 3.90) in the unadjusted model (Table 2).

CDKAL1 genetic marker was also associated with a significantly elevated risk of APO (OR: 2.51, 95%CI: 1.47, 4.28) after adjustment for traditional risk factors in the adjusted model 1. After further adjusting for GDM, the *CDKAL1* genetic marker exhibited a comparable risk for APO, with the OR (95%CI) was 2.52 (1.48, 4.30) (Table 3).

The *CDKAL1* genetic marker was associated with the risk of low birth weight (OR: 19.80, 95%CI: 2.15, 182) and macrosomia (OR: 2.40, 95%CI: 1.17, 4.93) but had no significant association with preterm birth ($P = 0.105$), after adjusting for traditional risk factors. After adjusting for GDM alongside the traditional risk factors, the *CDKAL1* genetic marker remained significantly associated with low birth weight and macrosomia, with the ORs showing no significant alterations. The adjusted ORs (95%CIs) were 20.62 (2.07, 205) for low birth weight, and 2.39 (1.16, 4.91) for macrosomia, respectively (Table 3).

Discussion

Our study revealed that the maternal *CDKAL1* gene variants was associated with the risk of APO and its components, including low birth weight and macrosomia, but not with preterm birth. Notably, this association was independent of GDM.

As a key risk factor gene for GDM, the potential associations of *CDKAL1* gene with both the short-term and long-term health outcomes of GDM should be a top priority in scientific research. However, this issue had

Table 1 Clinical characteristics of women with APO

Characteristic	Non-APO women (*n* = 321)	APO women (*n* = 93)	*P*
Variables during pregnancy			
Age, years	29 [27,31]	29 [27,31]	0.827
Pre-pregnancy BMI, kg/m^2	22.1 [20.0,24.9]	23.9 [21.6,26.2]	0.001
Systolic BP, mmHg	105 [100,110]	110 [100,120]	0.125
Diastolic BP, mmHg	70 [60,70]	70 [60,75]	0.119
Hypertension	4 (1.2)	4 (4.3)	0.145
Han ethnicity	310 (96.6)	92 (98.9)	0.401
Education > 12 years	180 (56.1)	47 (50.5)	0.409
Parity ≥ 1	15 (4.7)	8 (8.6)	0.230
Family history of diabetes in first degree relatives	29 (9.0)	10 (10.8)	0.766
GDM	155 (48.3)	52 (55.9)	0.239
Gestational age at registration, weeks	10.0 [9.0,11.0]	10.0 [9.0,12.0]	0.771
***CDKAL1*gene variants**			
rs141859146(A/G)			0.049
GG	315 (98.1)	87 (93.5)	
AG/AA	6 (1.9)	6 (6.5)	
rs7762612(C/T)			0.015
TT	272 (84.7)	68 (73.1)	
CT/CC	49 (15.3)	25 (26.9)	
rs4710944(T/C)			0.076
CC	312 (97.2)	86 (92.5)	
TC/TT	9 (2.8)	7 (7.5)	
Variables during delivery			
Infant female gender	140 (43.6)	33 (35.5)	0.200
Birth weight of neonates, g	3400 [3100,3650]	4050 [2850,4300]	< 0.001
Body height of neonates, cm	50 [50,51]	51 [49,52]	0.011
Delivery week, weeks	39.0 [38.0,40.0]	38.0 [36.0,40.0]	< 0.001

Abbreviations: APO, adverse pregnancy outcome; BMI, body mass index; BP, blood pressure; GDM, gestational diabetes mellitus; *CDKAL1*, cyclin-dependent kinase 5 regulatory subunit associated protein 1-like 1

Data was reported n (%) or medians (IQRs)

P for continuous variables derived from Wilcoxon rank sum test and for categorical variables derived from Chi-square test or Fisher's exact test

Table 2 Unadjusted odds ratios of maternal *CDKAL1* gene variants on APO

CDKAL1	OR (95% CI)	*P*
CDKAL1 gene variants		
rs141859146(A/G)		
AG/AA vs. GG	3.62 (1.14,11.5)	0.029
rs7762612(C/T)		
CT/CC vs. TT	2.04 (1.18,3.54)	0.011
rs4710944(T/C)		
TC/TT vs. CC	2.82 (1.02,7.80)	0.045
CDKAL1 genetic marker		
any of above variants	2.34 (1.41,3.90)	0.001

Abbreviations: APO, adverse pregnancy outcome; *CDKAL1*, cyclin-dependent kinase 5 regulatory subunit associated protein 1-like 1; OR, odds ratio; CI, confidence interval

Table 3 Odds ratio of maternal *CDKAL1* genetic marker on APO and its components

Outcomes	Adjusted model 1		Adjusted model 2	
	OR (95% CI)	*P*	OR (95% CI)	*P*
APO	2.51 (1.47,4.28)	< 0.001	2.52 (1.48,4.30)	< 0.001
Birth weight of neonates				
Normal birth weight	-	-	-	-
Low birth weight	19.80 (2.15,182)	0.008	20.62 (2.07,205)	0.010
Macrosomia	2.40 (1.17,4.93)	0.017	2.39 (1.16,4.91)	0.018
Preterm birth	2.28 (0.84,6.19)	0.105	2.36 (0.86,6.43)	0.094

Abbreviations: APO, adverse pregnancy outcome; *CDKAL1*, cyclin-dependent kinase 5 regulatory subunit associated protein 1-like 1; OR, odds ratio; CI, confidence interval

Adjusted model 1, adjusted for age, pre-pregnancy body mass index, family history of diabetes in first degree relatives, parity, education, Han ethnicity, hypertension, infant gender, and body height of neonates

Adjusted model 2, further adjusted for gestational diabetes mellitus, in addition to the variables in the adjusted model 1

not been explored in studies thus far. Currently, there were some studies focusing on the associations of the fetal *CDKAL1* gene with their birth weight, but the conclusions were inconsistent. An ongoing genome-wide association study based on 5,465 Caucasian children

showed that fetal *CDKAL1* rs7756992 was strongly associated with low birth weight [20], while a study based on the Mexican population indicated that rs7754840 in *CDKAL1* was not associated with birth weight [13]. After adjusting for confounding factors such as maternal age and BMI, we found that the maternal *CDKAL1* gene variants were significantly associated with APO, particularly the risks of low birth weight and macrosomia. Even after further adjusting for GDM, this association remained independent, indicating that the association between the *CDKAL1* gene and birth weight was independent of GDM. The biological mechanism by which the maternal *CDKAL1* gene influenced APO was still unclear, possibly involving its impact on insulin secretion and metabolic pathways, thereby altering blood glucose levels. Maternal blood glucose levels might potentially affect fetal growth and delivery outcomes [21]. Further research was needed to elucidate this mechanism. This new finding deepened our understanding of the genetic factors influencing pregnancy outcomes and emphasized the importance of considering genetic variants in research on maternal health.

The identification of the maternal *CDKAL1* gene variants as a risk factor for APO, independent of GDM, had important public health implications. Low birth weight was associated with postnatal metabolic disorders (such as obesity and insulin resistance), cardiovascular disease in adults, and diabetes [22, 23]. Similarly, preterm birth was considered a risk factor for diabetes [24] and macrosomia was regarded as a factor increased the risk of obesity later in life [25]. The detection of *CDKAL1* gene variants in pregnant women facilitated identifying pregnant women those at a high risk of APO, which could help prevent and manage APOs, through monitoring intrauterine growth and development of newborns and providing targeted prenatal care.

The study had several strengths and limitations. The strength was that it was a real-world cohort of pregnant women, including genetic variation and offspring information for pregnant women. A limitation of this study was that it was based on a cohort of pregnant women in Tianjin, and the research findings needed to be validated in other populations. Additionally, the IADPSG recommended using a one-step OGTT method to identify GDM, whereas we employed a two-step procedure for screening GDM in the current study, which might result in some pregnant women being missed. During our analysis, we accounted for internal environmental factors, including maternal age and pre-pregnancy BMI. However, owing to the lack of external environmental data in our database, we did not consider factors such as particulate matter 2.5, carbon dioxide, and other environmental variables.

In conclusion, *CDKAL1* gene variants were associated with the risk of APO, low birth weight and macrosomia, independent of GDM. *CDKAL1* gene variants might be useful markers for APO, low birthweight and macrosomia. Further research was warranted to explore the cause-effect association and underlying mechanisms between *CDKAL1* gene variants and fetal growth and development, which might lead to the discovery of new therapeutic strategies, such as the influence of phytochemicals on *CDKAL1* gene expression [26], thereby reducing the risk of APO in Chinese pregnant women.

Abbreviations

CDKAL1	cyclin-dependent kinase 5 regulatory subunit-associated protein 1-like 1
T2D	type 2 diabetes
GDM	gestational diabetes mellitus
APO	adverse pregnancy outcome
TWCHC	Clinical Research Ethics Committee of Tianjin Women's and Children's Health Center
GCT	glucose challenge test
OGTT	oral glucose tolerance test
IADPSG	International Association of Diabetes and Pregnancy Study Groups
BP	blood pressure
BMI	body mass index
SNP	single nucleotide polymorphism
SD	standard deviation
IQR	interquartile range
OR	odds ratio
CI	confidence interval

Supplementary Information

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Supplementary Material 1

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Author contributions

SY and MS analyzed the data and wrote the first draft. ZZ, J Li, J Leng, WL, J Liu, TZ, YQ, ZY, GH, and JM gave critical comments and edited the manuscript. XY and HW took full responsibility for the work, including the access to the data, and decision to submit.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was performed in line with the principles of the Declaration of Helsinki. Ethics approval was obtained from the Ethics Committee for Clinical Research of Tianjin Women and Children's Health Center (Ethics Approval number: 2009-02) and written informed consent was obtained from all pregnant women.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

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References

1. Pascoe L, Tura A, Patel SK, Ibrahim IM, Ferrannini E, Zeggini E, et al. Common variants of the novel type 2 diabetes genes CDKAL1 and HHEX/IDE are associated with decreased pancreatic β-Cell function. Diabetes. 2007;56:3101–4.
2. Association between polymorphisms in SLC30A8, HHEX, CDKN2A/B, IGF2BP2., FTO, WFS1, CDKAL1, KCNQ1 and type 2 diabetes in the Korean population| Journal of Human Genetics. https://www.nature.com/articles/jhg2008127. Accessed 30 Nov 2024.
3. Chistiakov DA, Potapov VA, Smetanina SA, Bel'chikova LN, Suplotova LA, Nosikov VV. The carriage of risk variants of CDKAL1 impairs beta-cell function in both diabetic and non-diabetic patients and reduces response to non-sulfonylurea and sulfonylurea agonists of the pancreatic KATP channel. Acta Diabetol. 2011;48:227–35.
4. Wang H, Yang W, Liu J, Leng J, Li W, Yu Z, et al. Serum concentrations of SFAs and CDKAL1 single-nucleotide polymorphism rs7747752 are related to an increased risk of gestational diabetes mellitus. Am J Clin Nutr. 2021;114:1698–707.
5. Pan Y, Huang X, Jiang X. Risk factors and prediction model for low-birth-weight infants born to women with gestational diabetes mellitus. Front Public Health. 2024;12:1432033.
6. Ye W, Luo C, Huang J, Li C, Liu Z, Liu F. Gestational diabetes mellitus and adverse pregnancy outcomes: systematic review and meta-analysis. BMJ. 2022;377:e067946.
7. La Verde M, De Franciscis P, Torre C, Celardo A, Grassini G, Papa R, et al. Accuracy of fetal biacromial diameter and derived ultrasonographic parameters to predict shoulder dystocia: A prospective observational study. Int J Environ Res Public Health. 2022;19:5747.
8. Deepa R, Van Schayck OCP, Babu GR. Low levels of vitamin D during pregnancy associated with gestational diabetes mellitus and low birth weight: results from the MAASTHI birth cohort. Front Nutr. 2024;11:1352617.
9. Catalano P, deMouzon SH. Maternal obesity and metabolic risk to the offspring: why lifestyle interventions May have not achieved the desired outcomes. Int J Obes. 2015;39:642–9.
10. La Verde M, Torella M, Riemma G, Narciso G, Iavarone I, Gliubizzi L, et al. Incidence of gestational diabetes mellitus before and after the Covid-19 lockdown: A retrospective cohort study. J Obstet Gynecol Res. 2022;48:1126–31.
11. Sheiner E. Gestational diabetes mellitus: Long-Term consequences for the mother and child grand challenge: how to move on towards secondary prevention?? Front Clin Diabetes Healthc. 2020;1:546256.
12. Sun X-F, Xiao X-H, Zhang Z-X, Liu Y, Xu T, Zhu X-L, et al. Positive association between type 2 diabetes risk alleles near CDKAL1 and reduced birthweight in Chinese Han individuals. Chin Med J. 2015;128:1873–8.
13. Aguilera-Venegas I-G, Mora-Peña J-S, Velazquez-Villafaña M, Gonzalez-Dominguez M-I, Barbosa-Sabanero G, Gomez-Zapata H-M, et al. Association of diabetes-related variants in ADCY5 and CDKAL1 with neonatal insulin, C-peptide, and birth weight. Endocrine. 2021;74:318–31.
14. Leng J, Shao P, Zhang C, Tian H, Zhang F, Zhang S, et al. Prevalence of gestational diabetes mellitus and its risk factors in Chinese pregnant women: A prospective Population-Based study in Tianjin, China. PLoS ONE. 2015;10:e0121029.
15. International Association of Diabetes and Pregnancy Study Groups Consensus Panel. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33:676–82.
16. Beaney T, Wang W, Schlaich MP, Schutte AE, Stergiou GS, Alcocer L, et al. Global blood pressure screening during the COVID-19 pandemic: results from the May measurement month 2021 campaign. J Hypertens. 2023;41:1446.
17. Hughes ZH, Hughes LM, Khan SS. Genetic contributions to risk of adverse pregnancy outcomes. Curr Cardiovasc Risk Rep. 2023;17:185–93.
18. Chen X, Wang Q, Zang H, Cong X, Shen Q, Chen L. First trimester sCD40L levels associated with adverse neonatal outcomes in euthyroid pregnant women with positive TPOAb. Front Endocrinol (Lausanne). 2023;14:1097991.
19. Anderson CA, Pettersson FH, Clarke GM, Cardon LR, Morris AP, Zondervan KT. Data quality control in genetic case-control association studies. Nat Protoc. 2010;5:1564–73.
20. Zhao J, Li M, Bradfield JP, Wang K, Zhang H, Sleiman P, et al. Examination of type 2 diabetes loci implicates CDKAL1 as a birth weight gene. Diabetes. 2009;58:2414–8.
21. Guo F, Long W, Zhou W, Zhang B, Liu J, Yu B. FTO, GCKR, CDKAL1 and CDKN2A/B gene polymorphisms and the risk of gestational diabetes mellitus: a meta-analysis. Arch Gynecol Obstet. 2018;298:705–15.
22. Vejrazkova D, Lukasova P, Vankova M, Bradnova O, Vacinova G, Vcelak J, et al. Gestational Diabetes - Metabolic risks of adult women with respect to birth weight. Physiol Res. 2015;64:S135–45.
23. Sun Y, Wang B, Yu Y, Wang Y, Tan X, Zhang J, et al. Birth weight, ideal cardiovascular health metrics in adulthood, and incident cardiovascular disease. Chin Med J. 2024;137:1160.
24. Li S, Zhang M, Tian H, Liu Z, Yin X, Xi B. Preterm birth and risk of type 1 and type 2 diabetes: systematic review and meta-analysis. Obes Rev. 2014;15:804–11.
25. Gillman MW, Rifas-Shiman S, Berkey CS, Field AE, Colditz GA. Maternal gestational diabetes, birth weight, and adolescent obesity. Pediatrics. 2003;111:e221–6.
26. Ghosh C, Das N, Saha S, Kundu T, Sircar D, Roy P. Involvement of Cdkal1 in the etiology of type 2 diabetes mellitus and microvascular diabetic complications: a review. J Diabetes Metab Disord. 2022;21:991–1001.

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