JDI Journal of Diabetes Investigation Open access
Official Journal of the Asian Association for the Study of Diabetes
ORIGINAL ARTICLE

Impact of family income on the development of gestational diabetes mellitus and the associated birth outcomes: A nationwide study

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Keywords
Birth outcomes, Family income, Gestational diabetes mellitus

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J Diabetes Investig 2025; 16: 51–59

doi: 10.1111/jdi.14288

ABSTRACT

Aims/Introduction: The relationship between economic disadvantages and the risk of developing gestational diabetes mellitus (GDM), as well as its impact on birth outcomes, remains uncertain.

Materials and Methods: From the Taiwan Maternal and Child Health Database, we identified 984,712 pregnant women between 1 January 2007 and 31 December 2018. Using propensity score matching, we selected 5,068 pairs of women across four income levels: very low, low, middle and high. We used a multivariable Cox regression model to assess the risk of GDM in these pregnant women and analyzed the birth outcomes.

Results: The mean age of the pregnant women was 30.89 years. We found no significant difference in GDM risk among pregnant women with different family income. However, newborns of women with GDM and very low-income were at higher risk for several adverse conditions, such as small for gestational age (adjusted odds ratio (aOR) 1.17, 95% confidence interval (CI) 1.04–1.31), large for gestational age (aOR 1.27, 95% CI 1.08–1.51), hypoxic–ischemic encephalopathy (aOR 3.19, 95% CI 1.15–8.86), respiratory distress (aOR 1.58, 95% CI 1.14–2. 19), congenital anomalies (aOR 1.32, 95% CI 1.08–1.62), jaundice requiring phototherapy or exchange transfusion (aOR 1.14, 95% CI 1.05–1.24) and so on.

Conclusions: This study found that low family income alone was not associated with GDM development. However, for a GDM pregnancy, pregnant women with lower income had worse birth outcomes. Improving maternal health and nutrition among low-income pregnant women with GDM might be critical to improving birth outcomes.

INTRODUCTION

Gestational diabetes mellitus (GDM) is a condition characterized by glucose intolerance that occurs during or after the 24th week of pregnancy. It is the most common pregnancy-related endocrinopathy[1,2]. Although the diagnostic criteria for GDM can vary worldwide, its prevalence is generally estimated to be between 1% to >30%[1,3]. Additionally, the incidence of GDM has gradually increased over the past few decades, possibly due to the westernization of diets and the escalating obesity epidemic[4]. The known risk factors for developing GDM include maternal obesity, advanced parity, GDM history, family history of diabetes mellitus and ethnicity[1,5]. Furthermore, some pregnant women might have had higher insulin resistance or lower insulin secretion before pregnancy due to various factors. During pregnancy, the increased demand for blood glucose and the secretion of placental hormones that increase insulin resistance

Received 9 July 2024; revised 15 July 2024; accepted 25 July 2024

might also lead them to the development of GDM[1,2]. The incidence of GDM is particularly high in the Middle East, certain North African countries, Southeast Asia and among some indigenous populations[1,6]. Economically disadvantaged pregnant women might have less access to healthy foods due to financial stress and/or be less able to maintain a healthy lifestyle, both of which can increase their risk of developing GDM[1,5,7].

There is strong evidence that even mild hyperglycemia in pregnant women increases the risk of fetal complications[1,8]. Pregnant women with GDM are more likely to have infants who are either larger or smaller than the typical gestational age. These infants might experience problems, such as hyperglycemia or hypoglycemia, respiratory distress, congenital defects, preterm birth, or even stillbirth[6,9,10]. Furthermore, the risk of poorer perinatal health is inversely related to socioeconomic status[11]. One study found that newborns born to high-income mothers have a lower risk of low birth weight (LBW) or preterm birth compared with those born to mothers of lower.

The perinatal period often represents a missed opportunity to connect women, particularly those from disadvantaged backgrounds, with needed services. Maternal mental health problems are more prevalent among those who are disadvantaged. Disadvantaged mothers might also receive less respectful treatment in private healthcare settings. This causes distrust, which reduces these women's motivation to seek care[12]. These factors might contribute to poorer birth outcomes among disadvantaged pregnant women. However, the available data relate to pregnant women in general. Whether poverty has a similar impact on birth outcomes for pregnant women with GDM remains unclear. Hence, the present study utilized the Taiwan Maternal and Child Health Database (TMCHD) to examine the impact of different family income levels on the risk of GDM in pregnant women. Additionally, we also investigated the relationship between different income levels and birth outcomes in the cohort of pregnant women with GDM.

MATERIALS AND METHODS

Data source

Taiwan launched its National Health Insurance (NHI) program in 1995. By 2000, the database covered approximately 99% of Taiwan's 23 million population. This comprehensive healthcare system includes 450 registered hospitals and 10,000 clinics. The NHI Research Database (NHIRD) stores detailed insurance information including age, sex, diagnoses, prescriptions and medical procedures. The recorded diagnoses are based on the International Classification of Diseases, 9th/10th Revision and Clinical Modifications (ICD-9/10-CM)[13]. The NHIRD also integrates mortality data from the National Death Registry.

To link health insurance data between children and their parents, the Taiwan Birth Registration Database, Birth Certificate Application (BCA), National Register of Death and the NHIRD were used to create the TMCHD[14]. This database provides comprehensive health data by including medical claims made by parents within 60 days of birth and linking parental medical records to their children. The TMCHD contains detailed records of live births including birthweight, gestational age and single or multiple birth/s. Encrypted parental identification numbers are also recorded. Additionally, maternal habits, such as smoking and alcohol use, along with the newborn's Apgar scores, are documented in the BCA. Parental outpatient and hospitalization records, and the causes of death (for infants and parents), are also included.

Data for the present study were sourced from the TMCHD, NHIRD and National Register of Death. The research adhered to the Declaration of Helsinki, and was approved by the Institutional Review Board of the National Health Research Institutes (EC1060704-E). To ensure privacy, identifiable healthcare provider information and patient data were encrypted before release. Therefore, the Research Ethics Committee waived the requirement for informed consent for this study.

Study population

Initially, 1,578,325 records of singletons ≥24 and ≤42 weeks' gestational age at delivery were identified from the Taiwan BCA data. After excluding individuals with type 1 diabetes mellitus (n = 900), type 2 diabetes mellitus diagnosed before pregnancy (n = 57,927), diagnosis of diabetes in early pregnancy (n = 4,523), delivery year <2007 or ≥2018 (n = 456,586), maternal age <18 or >50 years (n = 4,885) and incomplete demographic data (n = 68,792), a total of 984,712 pregnant women were identified between 2007 and 2018 (Figure 1).

Main outcomes

The first outcome of the present study was the incidence of GDM among pregnant women of very low, low, middle and high family income levels. GDM was identified using the ICD diagnostic codes from 24 weeks of gestation through to delivery (Table S1)[15]. Other main outcomes included small for gestational age (SGA), large for gestational age (LGA), hypoxic–ischemic encephalopathy, respiratory distress, congenital anomalies, jaundice requiring phototherapy or exchange transfusion, neonatal intensive care unit (NICU) admission, neonatal death (≤28 days), infant death (≤12 months),and common adverse outcomes associated with prematurity, including intraventricular hemorrhage, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, neonatal sepsis, patent ductus arteriosus, pharmacological patent ductus arteriosus treatment and patent ductus arteriosus surgery in pregnant women with GDM according to income levels[6,8,9,16]. Participants were continuously followed from the start of the study until the occurrence of an outcome, death or the end of the study on 31 December 2018.

Statistical analysis

We analyzed the maternal baseline characteristics, including age at delivery, delivery mode, urbanization level, obesity status, smoking status, alcohol consumption, family history of diabetes mellitus and comorbidities (such as hypertension, pre-

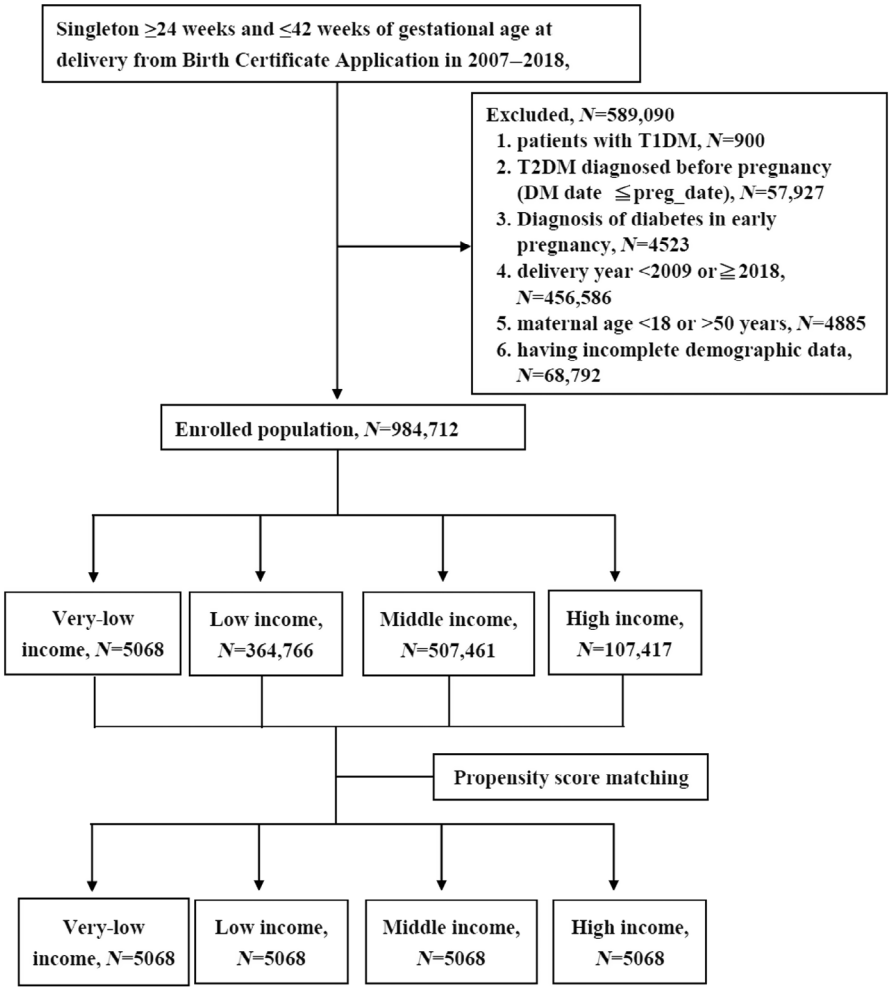

Figure 1 | Study participant flowchart. T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.

eclampsia, dyslipidemia, gout, polycystic ovary syndrome, rheumatoid arthritis, systemic lupus erythematosus and depression). Additionally, we considered the Charlson Comorbidity Index[17] and corticosteroid use during pregnancy among pregnant women from different income backgrounds (Table 1).

The risk of GDM and various birth outcomes are presented as events (%) during the observation period. We used the crude and adjusted models for analyses. Model 1 adjusted for age. Model 2 adjusted for factors in model 1 plus Charlson Comorbidity Index score, hypertension, dyslipidemia, gout, polycystic ovary syndrome, rheumatoid arthritis, systemic lupus erythematosus, depression and pre-eclampsia. Model 3 adjusted for factors in model 2 plus obesity, smoking, alcohol, family history of diabetes mellitus, corticosteroid use, mode of delivery and residence. The models were used to compare the risk of outcomes between pregnant women of different income levels. The results are presented as odds ratios (ORs) with 95% confidence intervals (CIs). We used the *P*-value to compare differences between pregnant women of different family income levels. A two-tailed *P*-value <0.05 was considered statistically significant. All statistical analyses were carried out with SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Baseline characteristics

The present study included 984,712 pregnant women identified from the Taiwan BCA between 2007 and 2018 (Figure 1). Among them, 5,068 (0.51%) pregnant women had very low family income, 364,766 (37.04%) had low income, 507,461 (51.53%) had middle income and 107,417 (10.91%) had high income. The mean (standard deviation) age of the pregnant women was 30.89 years (±4.86 years). At the time of delivery, 22.32% of the pregnant women were aged ≥35 years, and 34.6% delivered by cesarean section. Furthermore, 77.15% of the pregnant women lived in urban areas, 2.53% had pre-eclampsia, 1.58% had polycystic ovary syndrome and 5.28%

Table 1 | Baseline characteristics of pregnant women in all four income groups

Baseline characteristics	Total (n = 984,712)	Very-low (n = 5,068)	Low (n = 364,766)	Middle (n = 507,461)	High (n = 107,417)	P-value
Age, years (mean ± SD)	30.89 ± 4.86	26.7 ± 7.8	30.0 ± 5.2	31.0 ± 4.5	33.7 ± 4.1	<0.0001
Age groups, years, n (%)						
18–29	369,504 (37.52)	3,247 (64.07)	171,325 (46.97)	180,690 (35.61)	14,242 (13.26)	<0.0001
30–34	395,385 (40.15)	670 (13.22)	123,360 (33.82)	222,812 (43.91)	48,543 (45.19)	
35–50	219,823 (22.32)	1,151 (22.71)	70,081 (19.21)	103,959 (20.49)	44,632 (41.55)	
Gynecology delivery methods, n (%)						
Normal spontaneous delivery	646,344 (65.64)	3,515 (69.36)	234,706 (64.34)	338,447 (66.69)	69,676 (64.86)	<0.0001
Cesarean section	338,368 (34.36)	1,553 (30.64)	130,060 (35.66)	169,014 (33.31)	37,741 (35.14)	
Living area, n (%)						
Urban	759,740 (77.15)	3,372 (66.54)	259,080 (71.03)	402,205 (79.26)	95,083 (88.52)	
Suburban	203,295 (20.65)	1,279 (25.24)	94,793 (25.99)	96,371 (18.99)	10,852 (10.10)	<0.0001
Rural	21,677 (2.20)	417 (8.23)	10,893 (2.99)	8,885 (1.75)	1,482 (1.38)	
Behavior, n (%)						
Obesity status						
Overweight	833 (0.08)	5 (0.10)	341 (0.09)	415 (0.08)	72 (0.07)	<0.0001
Obesity	1,531 (0.16)	16 (0.32)	596 (0.16)	782 (0.15)	137 (0.13)	
Severe obesity	443 (0.04)	2 (0.04)	155 (0.04)	263 (0.05)	23 (0.02)	
Maternal smoking status	2,405 (0.24)	32 (0.63)	1,202 (0.33)	1,076 (0.21)	95 (0.09)	<0.0001
Maternal alcohol drinking	1,529 (0.16)	41 (0.81)	980 (0.27)	456 (0.09)	52 (0.05)	<0.0001
Family history of diabetes mellitus	63 (0.01)	0	21 (0.01)	28 (0.01)	14 (0.01)	0.0357
Comorbidity, n (%)						
Hypertension	2,866 (0.29)	44 (0.87)	1,110 (0.30)	1,372 (0.27)	340 (0.32)	<0.0001
Pre-eclampsia	24,875 (2.53)	166 (3.28)	9,366 (2.57)	12,919 (2.55)	2,424 (2.26)	<0.0001
Dyslipidemia	3,275 (0.33)	25 (0.49)	1,055 (0.29)	1,688 (0.33)	507 (0.47)	<0.0001
Gout	688 (0.07)	22 (0.43)	256 (0.07)	350 (0.07)	60 (0.06)	<0.0001
Polycystic ovary syndrome	15,605 (1.58)	31 (0.61)	4,284 (0.17)	8,862 (1.75)	2,428 (2.26)	<0.0001
Rheumatoid arthritis	881 (0.09)	7 (0.14)	298 (0.08)	459 (0.09)	117 (0.11)	0.0383
SLE	1,471 (0.15)	8 (0.16)	479 (0.13)	800 (0.16)	184 (0.17)	0.0032
Depression	2,106 (0.21)	43 (0.85)	988 (0.27)	919 (0.18)	156 (0.15)	<0.0001
CCI score ≥1	38,653 (3.93)	378 (7.46)	14,090 (3.86)	19,595 (3.86)	4,590 (4.27)	<0.0001
Corticosteroids use, n (%)	52,005 (5.28)	439 (8.66)	20,788 (5.70)	25,936 (5.11)	4,842 (4.51)	<0.0001

CCI, Charlson Comorbidity Index; GDM, gestational diabetes mellitus; SLE, systemic lupus erythematosus.

used corticosteroids during pregnancy (Table 1). After 1:1 propensity score matching, 5,068 pairs of pregnant women in each of the four income groups were analyzed.

GDM risk outcome

Before the propensity score matching, pregnant women with a high income showed an increased risk of GDM (aOR 1.00, 95% CI 1.00–1.04), pregnant women with a low (aOR 0.91, 95% CI 0.90–0.92) and very low (aOR 0.87, 95% CI 0.80–0.94) family income had a decreased risk compared with pregnant women from middle-income households (Table 2). Post-matching, the GDM risk among pregnant women with a high (aOR 1.08, 95% CI 0.96–1.21), low (aOR 0.97, 95% CI 0.86–1.08) and very low (aOR 0.90, 95% CI 0.80–1.02) family income was not significantly different to the pregnant women with a middle income (Table 2).

Neonatal outcomes as related to the pregnant women with GDM

In the pre-matched cohorts, newborns of women with GDM born to very low-income households showed a higher risk of SGA, LGA, hypoxic–ischemic encephalopathy, respiratory distress, congenital anomalies, jaundice requiring phototherapy or exchange transfusion, NICU admission, infant death (≤12 months),and common adverse outcomes associated with prematurity. Similarly, newborns of women with GDM born to low-income households had a higher risk of LGA, hypoxic–ischemic encephalopathy, neonatal hypoglycemia, congenital anomalies, jaundice requiring phototherapy or exchange transfusion, NICU admission, neonatal death and common adverse outcomes related to prematurity. Conversely, newborns of women with GDM born to high-income households had a significantly lower risk of SGA, LGA, jaundice requiring

Table 2 | The risk of gestational diabetes mellitus according to different family income levels

	N	Events (%)	Crude model		Adjusted model 1*		Adjusted model 2†		Adjusted model 3‡	
			Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Before matching	984,712									
Very-low	5,068	674 (13.30)	0.85 (0.78–0.92)	<0.0001	0.92 (0.85–1.00)	0.0601	0.92 (0.84–0.99)	0.0353	0.87 (0.80–0.94)	0.0007
Low	364,766	49,125 (13.47)	0.86 (0.85–0.87)	<0.0001	0.90 (0.89–0.91)	<0.0001	0.90 (0.89–0.91)	<0.0001	0.91 (0.90–0.92)	<0.0001
Middle	507,461	77,526 (15.28)	Reference		Reference		Reference		Reference	
High	107,417	18,860 (17.56)	1.18 (1.16–1.20)	<0.0001	1.05 (1.03–1.06)	<0.0001	1.05 (1.03–1.07)	<0.0001	1.02 (1.00–1.04)	0.0222
After matching	20,272									
Very-low	5,068	674 (13.30)	0.95 (0.85–1.06)	0.3541	0.95 (0.85–1.06)	0.3518	0.95 (0.84–1.06)	0.3331	0.90 (0.80–1.02)	0.0885
Low	5,068	680 (13.42)	0.96 (0.86–1.07)	0.4523	0.96 (0.85–1.07)	0.4501	0.96 (0.86–1.07)	0.4573	0.97 (0.86–1.08)	0.5578
Middle	5,068	706 (13.93)	Reference		Reference		Reference		Reference	
High	5,068	765 (15.09)	1.10 (0.98–1.23)	0.0962	1.10 (0.98–1.23)	0.0946	1.10 (0.98–1.23)	0.1048	1.08 (0.96–1.21)	0.1889

CI, confidence interval. *Adjusted model 1: adjust by age. †Adjusted model 2: adjust by model 1 variables, Charlson Comorbidity Index score, hypertension, dyslipidemia, gout, polycystic ovary syndrome, rheumatoid arthritis, systemic lupus erythematosus, depression and pre-eclampsia. ‡Adjusted model 3: adjust by model 2 variables, obesity, smoking, alcohol, family diabetes, corticosteroids use, gynecology delivery methods and living area.

phototherapy or exchange transfusion and neonatal death compared with those of mothers with GDM born to middle-income families (Table S2).

In the matched cohorts, newborns of mothers with GDM born to very low-income households had a higher risk of SGA (aOR 1.17, 95% CI 1.04–1.31), LGA (aOR 1.27, 95% CI 1.08–1.51), hypoxic–ischemic encephalopathy (aOR 3.19, 95% CI 1.15–8.86), respiratory distress (aOR 1.58, 95% CI 1.14–2.19), congenital anomalies (aOR 1.32, 95% CI 1.08–1.62), jaundice requiring phototherapy or exchange transfusion (aOR 1.14, 95% CI 1.05–1.24), NICU admission (aOR 1.44, 95% CI 1.19–1.73) and common adverse outcomes associated with prematurity (aOR 1.55, 95% CI 1.30–1.85). Newborns of women with GDM born to low-income families had a lower risk of jaundice requiring phototherapy or exchange transfusion (aOR 0.91.55, 95% CI 0.84–0.99), and newborns of women with GDM born to high-income households had a lower risk of SGA (aOR 0.88, 95% CI 0.78–0.99) compared with those of women with GDM born to middle-income families (Table 3).

DISCUSSION

In the present National Maternal and Child Health Cohort Study, we found that a low family income was not significantly associated with an increased risk of GDM among pregnant women. However, pregnant women with GDM and very low family income appeared to have worse birth outcomes compared with those from middle-income households. These adverse outcomes included higher rates of SGA, LGA, hypoxic–ischemic encephalopathy, respiratory distress, congenital anomalies, jaundice requiring phototherapy or exchange transfusion, NICU admission and other common complications associated with prematurity. Therefore, pregnant women with GDM and very low income should be encouraged and reminded to attend regular prenatal care visits. Importantly, healthcare professionals should carefully examine their newborns for any of the aforementioned adverse birth outcomes and provide appropriate treatment.

Currently, the known risk factors of GDM include maternal obesity, multiple pregnancies, a previous history of GDM and a family history of diabetes mellitus[4,5]. Previous studies have also found that some low-income countries and certain indigenous populations have a higher prevalence of GDM[1,6]. These raise the question of whether economically disadvantaged pregnant women might be more likely to develop GDM due to increased stress, fewer healthy behaviors and/or limited access to nutritious foods[5,7]. The results of this study showed that, after adjusting for several potential confounders in the pregnant women, low family income was not associated with a higher risk of GDM. The reason for this is unclear, but we speculate that although pregnant women might have low family income during pregnancy, they may not have had low income before pregnancy. Additionally, even if pregnant women had low family income and poorer dietary habits before becoming pregnant, they might adopt healthy behaviors during pregnancy and diligently follow health professional recommendations to ensure their unborn child's health[6,18]. These maternal efforts might have reduced the risk of developing GDM.

Evidence suggests that maternal GDM can have both immediate and long-term health consequences for both mother and child[1,8]. Infants born to women with GDM are more likely to be large or small for their gestational age, and might experience hypoglycemia or hyperglycemia, respiratory distress, congenital

Table 3 | Birth outcome risks of neonates born to mothers with gestational diabetes post-matching

	Events (%)	Crude model		Adjusted model 1*		Adjusted model 2†		Adjusted model 3‡		Adjusted model 4§	
		Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
SGA											
Very low	695 (13.71)	**1.18 (1.05–1.32)**	**0.0063**	**1.18 (1.05–1.32)**	**0.0062**	**1.17 (1.04–1.31)**	**0.0106**	**1.17 (1.04–1.31)**	**0.011**	**1.17 (1.04–1.31)**	**0.0117**
Low	562 (11.09)	0.92 (0.82–1.04)	0.2018	0.92 (0.82–1.04)	0.2016	0.92 (0.82–1.04)	0.1927	0.93 (0.82–1.05)	0.2541	0.93 (0.82–1.05)	0.2516
Middle	603 (11.90)	Reference		Reference		Reference		Reference		Reference	
High	536 (10.58)	***0.88 (0.77–0.99)***	***0.0352***	***0.88 (0.77–0.99)***	***0.0352***	***0.88 (0.78–0.99)***	***0.0425***	***0.88 (0.78–0.99)***	***0.0396***	***0.88 (0.78–0.99)***	***0.0422***
LGA											
Very low	337 (6.65)	**1.29 (1.09–1.52)**	**0.0025**	**1.29 (1.10–1.53)**	**0.0025**	**1.29 (1.09–1.53)**	**0.0026**	**1.27 (1.07–1.50)**	**0.006**	**1.27 (1.08–1.51)**	**0.0053**
Low	305 (6.02)	1.16 (0.98–1.38)	0.0849	1.16 (0.98–1.38)	0.0839	1.16 (0.98–1.38)	0.0803	1.12 (0.94–1.33)	0.2038	1.12 (0.94–1.33)	0.1983
Middle	265 (5.23)	Reference		Reference		Reference		Reference		Reference	
High	282 (5.56)	1.07 (0.90–1.27)	0.4551	1.07 (0.90–1.27)	0.4537	1.07 (0.90–1.27)	0.4513	1.09 (0.92–1.30)	0.3324	1.09 (0.91–1.30)	0.3460
Hypoxic ischemic encephalopathy											
Very low	15 (0.30)	**3.01 (1.09–8.28)**	**0.0332**	**3.01 (1.09–8.28)**	**0.0332**	**2.92 (1.06–8.07)**	**0.0386**	**3.18 (1.15–8.83)**	**0.0265**	**3.19 (1.15–8.86)**	**0.0258**
Low	8 (0.16)	1.60 (0.52–4.90)	0.4095	1.60 (0.52–4.90)	0.4096	1.60 (0.52–4.89)	0.4120	1.62 (0.53–4.95)	0.4014	1.62 (0.53–4.95)	0.4019
Middle	5 (0.10)	Reference		Reference		Reference		Reference		Reference	
High	13 (0.26)	2.60 (0.93–7.31)	0.0692	2.60 (0.93–7.31)	0.0692	2.64 (0.94–7.41)	0.0654	2.57 (0.91–7.21)	0.0738	2.56 (0.91–7.20)	0.0746
Respiratory distress											
Very low	105 (2.07)	**1.74 (1.26–2.39)**	**0.0007**	**1.74 (1.26–2.39)**	**0.0007**	**1.65 (1.19–2.27)**	**0.0024**	**1.58 (1.14–2.19)**	**0.0063**	**1.58 (1.14–2.19)**	**0.0064**
Low	64 (1.26)	1.05 (0.74–1.49)	0.7872	1.05 (0.74–1.49)	0.7871	1.05 (0.74–1.50)	0.7875	1.03 (0.72–1.47)	0.8632	1.03 (0.72–1.47)	0.8639
Middle	61 (1.20)	Reference		Reference		Reference		Reference		Reference	
High	78 (1.54)	1.28 (0.92–1.80)	0.1475	1.28 (0.92–1.80)	0.1473	1.30 (0.93–1.83)	0.1262	1.28 (0.91–1.79)	0.1617	1.28 (0.91–1.79)	0.1616
Neonatal hypoglycemia											
Very low	28 (0.55)	0.93 (0.56–1.56)	0.7923	0.93 (0.56–1.56)	0.7923	0.85 (0.51–1.44)	0.5491	0.75 (0.44–1.29)	0.2972	0.76 (0.44–1.30)	0.3140
Low	17 (0.34)	0.57 (0.31–1.03)	0.0607	0.57 (0.31–1.03)	0.0607	0.56 (0.31–1.02)	0.0598	0.55 (0.30–1.01)	0.0524	0.55 (0.30–1.01)	0.0531
Middle	30 (0.59)	Reference		Reference		Reference		Reference		Reference	
High	19 (0.37)	0.63 (0.36–1.12)	0.1184	0.63 (0.36–1.12)	0.1183	0.64 (0.36–1.14)	0.1301	0.64 (0.36–1.14)	0.1316	0.64 (0.36–1.14)	0.1315
Congenital anomaly											
Very low	228 (4.50)	**1.31 (1.07–1.60)**	**0.0084**	**1.31 (1.07–1.60)**	**0.0084**	**1.32 (1.08–1.62)**	**0.0068**	**1.32 (1.08–1.62)**	**0.0072**	**1.32 (1.08–1.62)**	**0.0071**
Low	200 (3.95)	1.14 (0.93–1.40)	0.2075	1.14 (0.93–1.40)	0.2072	1.15 (0.93–1.41)	0.1989	1.15 (0.93–1.41)	0.1969	1.15 (0.93–1.41)	0.1959
Middle	176 (3.47)	Reference		Reference		Reference		Reference		Reference	
High	183 (3.61)	1.04 (0.84–1.29)	0.7069	1.04 (0.84–1.29)	0.7066	1.04 (0.84–1.29)	0.7118	1.03 (0.84–1.28)	0.7596	1.03 (0.84–1.28)	0.7619
Birth trauma (shoulder dystocia, brachial plexus injury, clavicular fracture)											
Very-low	16 (0.32)	0.80 (0.41–1.54)	0.5051	0.80 (0.41–1.54)	0.5051	0.84 (0.43–1.62)	0.5976	0.58 (0.29–1.16)	0.1213	0.60 (0.30–1.20)	0.1507
Low	16 (0.32)	0.80 (0.41–1.54)	0.5051	0.80 (0.41–1.54)	0.5051	0.81 (0.42–1.57)	0.5303	0.76 (0.39–1.47)	0.4094	0.78 (0.40–1.51)	0.4576
Middle	20 (0.39)	Reference		Reference		Reference		Reference		Reference	
High	25 (0.49)	1.25 (0.69–2.26)	0.4560	1.25 (0.69–2.26)	0.4560	1.22 (0.67–2.19)	0.5186	1.16 (0.64–2.10)	0.6339	1.15 (0.63–2.10)	0.6412
Jaundice s/p phototherapy or exchange transfusion											
Very low	2023 (39.92)	**1.17 (1.08–1.27)**	**0.0001**	**1.17 (1.08–1.27)**	**0.0001**	**1.17 (1.08–1.26)**	**0.0002**	**1.14 (1.05–1.24)**	**0.0019**	**1.14 (1.05–1.24)**	**0.0014**
Low	1725 (34.04)	***0.91 (0.84–0.99)***	***0.0221***	***0.91 (0.84–0.99)***	***0.0221***	***0.91 (0.84–0.99)***	***0.0223***	***0.91 (0.84–0.99)***	***0.0271***	***0.91 (0.84–0.99)***	***0.0291***
Middle	1835 (36.21)	Reference		Reference		Reference		Reference		Reference	
High	1843 (36.37)	1.01 (0.93–1.09)	0.8687	1.01 (0.93–1.09)	0.8687	1.01 (0.93–1.09)	0.8723	1.01 (0.93–1.09)	0.9011	1.00 (0.92–1.09)	0.9536
NICU admission											
Very low	293 (5.78)	**1.44 (1.20–1.73)**	**<0.0001**	**1.44 (1.20–1.73)**	**<0.0001**	**1.41 (1.17–1.69)**	**0.0003**	**1.43 (1.19–1.73)**	**0.0002**	**1.44 (1.19–1.73)**	**0.0002**
Low	202 (3.99)	0.98 (0.80–1.19)	0.8008	0.98 (0.80–1.19)	0.8005	0.97 (0.80–1.19)	0.7784	**0.98 (0.80–1.19)**	0.8102	**0.98 (0.80–1.19)**	0.8116
Middle	207 (4.08)	Reference		Reference		Reference		Reference		Reference	
High	198 (3.91)	0.96 (0.78–1.17)	0.6481	0.96 (0.78–1.17)	0.6477	0.96 (0.79–1.17)	0.6930	0.94 (0.77–1.14)	0.5203	0.94 (0.77–1.14)	0.5173
Neonatal death (≤28 days)											
Very low	7 (0.14)	0.88 (0.32–2.41)	0.7963	0.88 (0.32–2.41)	0.7962	0.87 (0.31–2.43)	0.7923	0.91 (0.32–2.56)	0.8505	0.91 (0.32–2.59)	0.8656
Low	9 (0.18)	1.13 (0.43–2.92)	0.8083	1.13 (0.43–2.92)	0.8083	1.15 (0.44–2.99)	0.7768	1.17 (0.45–3.06)	0.7435	1.18 (0.45–3.07)	0.7393
Middle	8 (0.16)	Reference		Reference		Reference		Reference		Reference	
High	8 (0.16)	1.00 (0.38–2.67)	1.0000	1.00 (0.38–2.67)	1.0000	1.01 (0.38–2.69)	0.9922	0.97 (0.36–2.60)	0.9510	0.97 (0.36–2.61)	0.9540

Table 3. (*Continued*)

	Events (%)	Crude model		Adjusted model 1*		Adjusted model 2†		Adjusted model 3‡		Adjusted model 4§	
		Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Infant death (≤12 months)											
Very low	25 (0.49)	1.47 (0.79–2.73)	0.2189	1.47 (0.79–2.73)	0.2189	1.48 (0.80–2.75)	0.2155	1.56 (0.83–2.93)	0.1638	1.57 (0.84–2.94)	0.1602
Low	17 (0.34)	1.00 (0.51–1.96)	1.0000	1.00 (0.51–1.96)	1.0000	1.01 (0.51–1.97)	0.9865	1.03 (0.52–2.02)	0.9394	1.03 (0.52–2.02)	0.9373
Middle	17 (0.34)	Reference		Reference		Reference		Reference		Reference	
High	12 (0.24)	0.71 (0.34–1.48)	0.3549	0.71 (0.34–1.48)	0.3549	0.71 (0.34–1.49)	0.3636	0.69 (0.33–1.46)	0.3334	0.69 (0.33–1.45)	0.3311
Common adverse outcomes in prematurity¶											
Very low	351 (6.93)	**1.58 (1.33–1.88)**	**<0.0001**	**1.58 (1.33–1.88)**	**<0.0001**	**1.55 (1.31–1.84)**	**<0.0001**	**1.55 (1.30–1.84)**	**<0.0001**	**1.55 (1.30–1.85)**	**<0.0001**
Low	266 (5.25)	1.18 (0.98–1.41)	0.0799	1.18 (0.98–1.41)	0.0798	1.18 (0.98–1.41)	0.0789	1.18 (0.99–1.42)	0.0703	1.18 (0.99–1.42)	0.0692
Middle	228 (4.50)	Reference		Reference		Reference		Reference		Reference	
High	250 (4.93)	1.10 (0.92–1.32)	0.3028	1.10 (0.92–1.32)	0.3027	1.11 (0.92–1.33)	0.2806	1.09 (0.91–1.31)	0.3539	1.09 (0.91–1.31)	0.3608

GDM, gestational diabetes mellitus; LGA, large for gestational age; NICU, neonatal intensive care unit; SGA, small for gestational age. *Adjusted model 1: adjust by age. †Adjusted model 2: adjust by model 1 variables, Charlson Comorbidity Index score, hypertension, dyslipidemia, gout, polycystic ovary syndrome, rheumatoid arthritis, systemic lupus erythematosus, depression, and pre-eclampsia. ‡Adjusted model 3: adjust by model 2 variables, obesity, smoking, alcohol, family diabetes, corticosteroids use, gynecology delivery methods and living area. §Adjusted model 4: adjust by model 3 variables and gestational diabetes mellitus. ¶Common adverse outcomes in prematurity include intraventricular hemorrhage, retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, newborn sepsis, patent ductus arteriosus (PDA), pharmacological PDA treatment and PDA surgery. bold and bold italics values indicate statistically siginficant values.

defects, hypoglycemic encephalopathy, preterm birth and stillbirth[6,8,9]. A recent systemic review also found that in Southeast Asia, children born to women with GDM are prone to macrosomia, LBW, intrauterine growth retardation, neonatal hypoglycemia and stillbirth[10]. Previous studies have shown that newborns born to high-income women have a lower risk of LBW and preterm birth than those born to women of lower socioeconomic status[11,12].

Disadvantaged pregnant women might have less access to quality prenatal care and medical services, which can lead to poorer birth outcomes[12]. A systematic review highlighted that pregnant women with GDM in indigenous populations have worse birth outcomes, including higher rates of macrosomia, congenital anomalies and NICU admission[6]. The present study further showed that newborns of women with GDM born to very low-income households had worse neonatal outcomes, with higher risks of SGA, LGA, hypoxic ischemic encephalopathy, respiratory distress, congenital anomalies, jaundice requiring phototherapy or exchange transfusion, NICU admissions and other common complications associated with prematurity than those of women with GDM born to middle-income families.

The possible explanation for why pregnant women with GDM and very low family income have poorer birth outcomes might be that these women are more likely to have lived in poverty both during and before pregnancy. This situation often leads to higher consumption of high-calorie or high-sugar foods, less exercise and greater life stress, which contributes to higher metabolic issues and insulin resistance[19–21]. As a result, disadvantaged pregnant women with GDM might struggle with poorer glycemic control or require insulin treatment more often than pregnant women with GDM from a middle-income background[22]. Birth outcomes are highly sensitive to maternal blood glucose levels. Even small increases in blood glucose (no specific threshold) can lead to poorer outcomes[1,9]. Furthermore, pregnant women with GDM and very low income might not attend regular prenatal care due to economic pressures[11]. They might also face inequitable access to healthcare, which in turn, compromises self-confidence to address pregnancy complications promptly, resulting in poorer birth outcomes[12,23].

The results of the present study have relevant clinical implications. First, as a nationwide cohort study of pregnant women and newborns, selection biases are minimized. The database provides data for many important maternal and infant variables. This allows us to match and adjust our analyses to minimize the impact of confounding factors. Second, the large study population facilitated stratified analyses by different family income levels. This contributed insights into the relationship between family income, GDM risk and birth outcomes. Third, our study suggests that family income might not be significantly associated with the occurrence of GDM, but has a clear impact on the birth outcomes of infants born to women with GDM. In the future of precision medicine, family income might not need to be considered as a risk factor for the development of GDM. However, family income should be considered when assessing birth outcomes of infants born to mothers with GDM[24]. Fourth, this study

suggests that women with GDM and low family income are more likely to have babies with abnormalities. Consequently, encouraging these women to adopt a healthy diet and appropriate lifestyle habits, as well as using medication to better control their blood glucose is paramount[25,26]. Regular reminders and prenatal checkups, along with careful examination and care of the newborns, must be considered.

The present study had some limitations. First, data relating to family history, exercise, diet and education were not available from the database, which might affect the assessment of maternal and infant health. Additionally, data on blood glucose and hemoglobin A1C levels were lacking. Hence, we could not assess the GDM severity of our participants. To reduce confounding and ensure a balanced comparison of clinical outcomes for both mothers and infants, we adjusted for relevant variables, such as maternal demographics, comorbidities, corticosteroid use, baseline characteristics and neonatal clinical conditions. Second, this study focused on a Taiwanese population, which might limit its generalizability to other ethnic groups. However, the findings might be relevant to other Asian populations at a high risk of GDM. Third, because of the observational nature of the study, unknown or unmeasured confounders might have influenced our results. Only associations could be established and not causality. Further prospective studies are needed to confirm our findings.

This nationwide, population-based cohort study found that low family income alone was not associated with a higher risk of developing GDM in pregnant women. However, those with GDM and very low income had worse birth outcomes than those with middle income. Improving maternal health and nutrition in pregnant women with GDM from a low-income background might be critical for improving the birth outcomes of infants, and breaking the intergenerational cycle of metabolic disorders.

ACKNOWLEDGMENTS

This study was based on data from the NHIRD provided by the NHI Administration, Taiwan. The interpretation of data and conclusions reported do not represent those of the NHI Administration.

FUNDING

This work was partially supported by grants from the National Health Research Institutes, Taiwan. This funding agency had no role in the study design, data collection and analysis, decision to publish or manuscript preparation.

DISCLOSURE

The authors declare no conflict of interest. Hwu, Chii-Min is an Editorial Board member of *Journal of Diabetes Investigation* and a co-author of this article. To minimize bias, they were excluded from all editorial decision-making related to the acceptance of this article for publication.

Approval of the research protocol: The study was approved by the Research Ethics Committee of the National Health Research Institutes, no: EC1060704-E.
Informed consent: To ensure privacy, identifiable healthcare provider information and patient data were encrypted before data release. Therefore, the Research Ethics Committee waived the requirement for informed consent for this study.
Approval date by the Research Ethics Committee: 8 April, 2019.
Animal studies: N/A.

DATA AVAILABILITY STATEMENT

Study data are available from the National Health Insurance Research Database (NHIRD), published by the Taiwan National Health Insurance (NHI) Administration. The data used in this study cannot be made available in the paper, supplemental files or a public repository due to the "Personal Information Protection Act" executed by the Taiwan government starting in 2012. Requests for data can be sent as a formal proposal to the NHIRD Office (https://dep.mohw.gov.tw/DOS/cp-2516-3591-113.html) or by email to stsung@mohw.gov.tw.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Table S1. International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification (ICD-9/10-CM) codes for diseases used in this study.

Table S2. Birth outcome risks of neonates born to mothers with GDM pre-matching.