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Comparison of maternal morbidity and medical costs during pregnancy and delivery between patients with gestational diabetes and patients with pre-existing diabetes

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Abstract

Aims To evaluate the effects of gestational diabetes and pre-existing diabetes on maternal morbidity and medical costs, using data from the Korea National Health Insurance Claims Database of the Health Insurance Review and Assessment Service.

Methods Delivery cases in 2010, 2011 and 2012 (459 842, 442 225 and 380 431 deliveries) were extracted from the Health Insurance Review and Assessment Service database. The complications and medical costs were compared among the following three pregnancy groups: normal, gestational diabetes and pre-existing diabetes.

Results Although, the rates of pre-existing diabetes did not fluctuate (2.5, 2.4 and 2.7%) throughout the study, the rate of gestational diabetes steadily increased (4.6, 6.2 and 8.0%). Furthermore, the rates of pre-existing diabetes and gestational diabetes increased in conjunction with maternal age, pre-existing hypertension and cases of multiple pregnancy. The risk of pregnancy-induced hypertension, urinary tract infections, premature delivery, liver disease and chronic renal disease were greater in the gestational diabetes and pre-existing diabetes groups than in the normal group. The risk of venous thromboembolism, antepartum haemorrhage, shoulder dystocia and placenta disorder were greater in the pre-existing diabetes group, but not the gestational diabetes group, compared with the normal group. The medical costs associated with delivery, the costs during pregnancy and the number of in-hospital days for the subjects in the pre-existing diabetes group were the highest among the three groups.

Conclusions The study showed that the rates of pre-existing diabetes and gestational diabetes increased with maternal age at pregnancy and were associated with increases in medical costs and pregnancy-related complications.

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Introduction

Gestational diabetes mellitus is associated with maternal morbidity and complications such as pre-eclampsia, premature rupture of membranes and Caesarean section [1]. The prevalence of gestational diabetes has recently escalated and may be related to increases in maternal age, the glaring obesity epidemic or increasingly sedentary lifestyles [2]. In 2007, gestational diabetes increased national medical costs in the USA by $636 million [3] and is strongly correlated with an increased risk of developing Type 2 diabetes later in life for both mother and child [2,4]. The rate of pre-existing diabetes mellitus before pregnancy has also increased recently as a result of the increasing prevalence of obesity and diabetes among females of reproductive age [4]. Pre-existing diabetes is associated with complications during pregnancy, including increased rates of macrosomia, congenital anomaly and Caesarean section [5–8]. The clinical and social significance of gestational diabetes and pre-existing diabetes has also become an important issue in the arena of public health because these diseases can cause maternal complications and influence the development of the

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What's new

- Many studies have shown that gestational diabetes and pre-existing diabetes aggravate complications during pregnancy. This study investigated the complications associated with normal pregnancy, pregnancy with gestational diabetes and pregnancy with pre-existing diabetes using data extracted from national health insurance claims.
- The findings showed that the prevalence of gestational diabetes increased rapidly during the period studied, both gestational diabetes and pre-existing diabetes were associated with several adverse pregnancy outcomes and complications, and the medical costs associated with pre-existing diabetes were higher than those for gestational diabetes.
- These data could aid in the development of healthcare policies that may reduce complications related to gestational diabetes and pre-existing diabetes during pregnancy.

offspring during the pregnancy and later in life. The medical costs and social burdens caused by gestational diabetes and pre-existing diabetes are also problematic.

A large number of studies have investigated the maternal morbidity and medical costs associated with gestational diabetes and pre-existing diabetes. In Korea, rates of gestational diabetes and pre-existing diabetes have recently been increasing, but few studies have evaluated these diseases specifically in Korean females. In the present study, therefore, we investigated the maternal morbidity and medical costs associated with gestational diabetes and pre-existing diabetes in Korean females of reproductive age relative to female subjects without gestational diabetes or pre-existing diabetes using information from the Korea National Health Insurance Claims Database of the Health Insurance Review and Assessment Service.

Patients and methods

Data source

Under the National Health Insurance System, all Koreans are beneficiaries of medical coverage as either an employee or as a member of a community [9]. The Health Insurance Review and Assessment Service database contains information concerning the claims of ~50 million Koreans [9] but, because it is a claims database, clinically relevant information such as smoking, alcohol use, body weight and height were not available.

Study subjects and definition of variables

Data from subjects aged 15–49 years who gave birth from 2010 to 2012 were extracted for this study using the diagnosis and procedure codes from the International Classification of Diseases 10th revision (ICD-10). The procedure codes related to delivery were used to classify each delivery (Table S1). A delivery of twins counted as one delivery. There were 459 842 deliveries in 2010, 461 037 in 2011 and 471 752 in 2012. If a subject delivered more than once during the 3-year study period, then only the first delivery was included in the present study to remove the possible correlations among deliveries in the same subject. After excluding the cases in which a subject delivered more than once during 3 years, data from 459 842 deliveries in 2010, 442 225 deliveries in 2011 and 380 431 deliveries in 2012 were analysed. To evaluate the total medical costs and to analyse the complications associated with pregnancy and delivery, the pregnancy period was estimated to be 10 months before the date of each subject's delivery.

All delivery cases were categorized into three pregnancy groups, normal, gestational diabetes and pre-existing diabetes, according to the ICD-10 codes. The pre-existing diabetes group was classified by the following codes: pre-existing diabetes and insulin-dependent during pregnancy (O24.0), pre-existing diabetes and non-insulin-dependent during pregnancy (O24.1), pre-existing malnutrition-related diabetes during pregnancy (O24.2), unspecified pre-existing diabetes during pregnancy (O24.3), unspecified diabetes during pregnancy (O24.9), insulin-dependent diabetes (E10), non-insulin-dependent diabetes (E11), other specified diabetes (E13) and unspecified diabetes (E14). Subjects were classified as having gestational diabetes if diabetes initially manifested during pregnancy (O24.4) and all others who did not have any codes related to diabetes were classified as the normal group.

The prevalence rates of pre-existing diabetes and gestational diabetes were estimated by dividing the number of females with either pre-existing diabetes or gestational diabetes giving birth in that year by the total number of females giving birth in that year [4]. Complications were defined according to the ICD-10 codes (Table S2) and were based on the definitions of complications from a previous study by Lutomski *et al.* [10].

Statistical analysis

All statistical analyses were performed using the Statistical Program for SAS, version 9.2 (SAS institute Inc.; Cary, NC, USA). The medical costs and in-hospital days for all groups are presented as means ± SD, categorical variables were compared using the chi-squared test, and continuous variables were compared using a one-way ANOVA in conjunction with Tukey's *post hoc* test. To evaluate the effect of pre-existing diabetes or gestational diabetes on pregnancy-related complications, we constructed three separate models for analyses by logistic regression analysis: (1) an unadjusted model; (2) an age-adjusted model; and (3) a multivariate-adjusted model that adjusted for maternal age, multiple

pregnancy and pre-existing hypertension, which differed in rates among the normal, pre-existing diabetes and gestational diabetes groups. Additionally, in analyses of shoulder dystocia, preterm delivery and prolonged pregnancy (> 42 weeks) as adverse pregnancy outcomes, we adjusted for maternal age, multiple pregnancy, pre-existing hypertension and Caesarean section. The risks for each maternal complication were presented as odds ratios with 95% CIs and a P value < 0.05 was taken to indicate statistical significance.

Results

During the 3 years of the study (2010, 2011 and 2012), the annual rate of deliveries complicated by pre-existing diabetes remained relatively stable, whereas the annual rate of deliveries complicated by gestational diabetes showed an increasing trend (4.6, 6.2 and 8.0%, respectively; Table 1). The rates of gestational diabetes and pre-existing diabetes increased with age (Table 1) and in subjects aged ≥ 35 years old, the rates of gestational diabetes and pre-existing diabetes were 7.1–11.3% and 4.1–4.7%, respectively, over the 3-year study period. The incidence of gestational diabetes was greater than the incidence of pre-existing diabetes in all age groups. The pre-existing diabetes and gestational diabetes groups had a higher rate of older subjects (≥ 35 years) as well as higher rates of Caesarean section, pre-existing hypertension and multiple pregnancy compared with the normal group (Table 2).

The effect of pre-existing diabetes or gestational diabetes on pregnancy-related complications is shown in Table 3. The unadjusted risk for pregnancy-induced hypertension, with or without significant proteinuria, and eclampsia in the gestational diabetes and pre-existing diabetes groups were greater than in the normal group. After adjusting for age, the risk of pregnancy-induced hypertension, with or without significant proteinuria, and eclampsia were greater in the gestational diabetes and pre-existing diabetes groups than in the normal group, but the risk of eclampsia was not greater in the gestational diabetes than in the normal group in the multivariate-adjusted model. Compared with subjects in the normal group, the risk of genitourinary tract infections was greater in the gestational diabetes and pre-existing diabetes groups regardless of adjusting. Only subjects in the pre-existing diabetes group were at a greater risk of embolism/deep vein thrombosis and only those in the gestational diabetes group were at a greater risk of puerperal sepsis, regardless of adjusting. The risk of antepartum haemorrhage was greater and the risk of postpartum haemorrhage was lower in the pre-existing diabetes group, regardless of adjusting. The risk of pelvic and perennial trauma was lower in the gestational diabetes and pre-existing diabetes groups relative to the normal group and the risk of uterine rupture did not differ among the groups. The risk of shoulder dystocia was greater in the pre-existing diabetes group compared with the normal group, regardless of adjusting.

Table 1 Rates of deliveries complicated by gestational diabetes and pre-existing diabetes per 100 deliveries in South Korea, 2010–2012, stratified by maternal age group

	2010			2011			2012		
Age	Deliveries, *n*	Gestational diabetes, *n* (%)	Pre-existing diabetes, *n* (%)	Deliveries, *n*	Gestational diabetes, *n* (%)	Pre-existing diabetes, *n* (%)	Deliveries, *n*	Gestational diabetes, *n* (%)	Pre-existing diabetes, *n* (%)
15–20 years	3339	23 (0.7)	19 (0.6)	3448	21 (0.6)	18 (0.5)	2871	38 (1.3)	24 (0.8)
21–30 years	166 342	4255 (2.6)	2,371 (1.4)	149 122	5044 (3.4)	2221 (1.5)	119 389	5335 (4.5)	1894 (1.6)
31–40 years	281 279	15 974 (5.7)	8,625 (3.1)	279 671	21 188 (7.6)	7682 (2.8)	248 033	23 787 (9.6)	7482 (3.0)
41–49 years	8882	733 (8.3)	599 (6.7)	9984	1037 (10.4)	600 (6.0)	10 138	1281 (12.6)	672 (6.6)
≥ 35 years	78 591	5554 (7.1)	3,596 (4.6)	80 615	7410 (9.2)	3327 (4.1)	74 448	8393 (11.3)	3481 (4.7)
Total	459 842	20 985 (4.6)	11,614 (2.5)	442 225	27 290 (6.2)	10 521 (2.4)	380 431	30 441 (8.0)	10 072 (2.7)

Table 2 Rates of pregnancy-induced hypertension, multiple pregnancy and Caesarean section among deliveries to subjects with and without gestational diabetes and pre-existing diabetes in South Korea, stratified by year of delivery

Year	Group	Age ≥ 35 years, *n* (%)	Pre-existing hypertension, *n* (%)	Multiple pregnancy, *n* (%)	Caesarean section, *n* (%)
2010	Normal (*n* = 427 243)	69 441 (16.3)	4730 (1.1)	5865 (1.4)	151 106 (35.4)
	Gestational diabetes (*n* = 20 985)	5554 (26.5)	517 (2.5)	428 (2.0)	8965 (42.7)
	Pre-existing diabetes (*n* = 11 614)	3596 (31.0)	763 (6.6)	307 (2.6)	5858 (50.4)
	*P**	< 0.001	< 0.001	< 0.001	< 0.001
2011	Normal (*n* = 404 414)	69 878 (17.3)	4137 (1.0)	5867 (1.5)	144 348 (35.7)
	Gestational diabetes (*n* = 27 290)	7410 (27.2)	505 (1.9)	609 (2.2)	11 358 (41.6)
	Pre-existing diabetes (*n* = 10 521)	3327 (31.6)	702 (6.7)	232 (2.2)	5417 (51.5)
	*P**	< 0.001	< 0.001	< 0.001	< 0.001
2012	Normal (*n* = 339,918)	62 574 (18.4)	3301 (1.0)	5886 (1.7)	125 617 (37.0)
	Gestational diabetes (*n* = 30 441)	8393 (27.6)	591 (1.9)	744 (2.4)	12 655 (41.6)
	Pre-existing diabetes (*n* = 10 072)	3481 (34.6)	653 (6.5)	356 (3.5)	5186 (51.5)
	*P**	< 0.001	< 0.001	< 0.001	< 0.001

*Differences among normal, gestational diabetes and pre-existing diabetes pregnancy groups, compared using the chi-squared test.

Also relative to the normal group, the risks of premature separation of the placenta, placenta previa and placenta disorders were greater in the pre-existing diabetes group, regardless of adjusting. The risks of preterm delivery and premature rupture of membranes were greater in both the gestational diabetes and pre-existing diabetes groups, while the risk of prolonged pregnancy was lower relative to that in the normal group, regardless of adjusting. The risks of liver disease and chronic renal disease were greater in the gestational diabetes and pre-existing diabetes groups compared with the normal group, but the risk of acute renal complication was higher only in subjects in the pre-existing diabetes group, regardless of adjusting.

The total medical costs during the pregnancy period, which was defined as the 10-month period before the delivery day, were also analysed (Fig. 1a). The total cost during pregnancy for subjects in the pre-existing diabetes group was the highest (normal: $1,310; gestational diabetes: $1,477 pre-existing diabetes; $1,760). The total medical costs during pregnancy were also stratified based on delivery type; the total medical costs of the pre-existing diabetes group were highest in the both the vaginal delivery and Caesarean section categories. Likewise, the delivery-only costs (costs after admission for delivery) were analysed for each group; the delivery-only costs associated with the pre-existing diabetes group were the highest among three groups (Fig. 1b). After stratifying by delivery type, the delivery-only costs for both vaginal delivery and Caesarean section were highest in the pre-existing diabetes group. The mean ± SD number of in-hospital days associated with delivery calculated for the normal, gestational diabetes and pre-existing diabetes groups were 4.65 ± 2.67, 4.89 ± 2.76 and 5.39 ± 3.24 days, respectively with the pre-existing diabetes and gestational diabetes subjects having significantly longer stays than the normal group ($P < 0.001$).

Discussion

The findings of the present study show that 4.6–8.0% of deliveries in Korea were affected by gestational diabetes and the rate has increased rapidly. Several recent studies of the Korean population have found that gestational diabetes develops in 2–5% of females giving birth [12], while the incidence of gestational diabetes in various different ethnic populations has been reported to be 3–6% [11]. It is possible that this rapid increase in the incidence of gestational diabetes is attributable to increasing maternal age and/or obesity or to an improved capability of detecting gestational diabetes because the screening procedure for this disease was recently generalized [2,4]. Although the rates differ according to race, pregnant subjects with pre-existing diabetes may have either Type 1 diabetes (incidence: 0.5%) or Type 2 diabetes (incidence: 2%; [11]). In the present 3-year study, 2.4–2.7% of deliveries were affected by pre-existing diabetes, but this rate did not significantly change throughout the study even though gestational diabetes rates increased every year. A health insurance claims database was used to gather these data, and the number of deliveries rather than the exact number of pregnancies was used to calculate the incidence rates of gestational diabetes and pre-existing diabetes. Despite this limitation, our data suggest that the rate of gestational diabetes increased every year.

Our findings of higher rates of gestational diabetes and pre-existing diabetes among deliveries to women in older age groups are consistent with previous observations [13,14]. Accordingly, our study showed that the rate of women aged ≥ 35 years old was greater in the gestational diabetes and pre-existing diabetes than in the normal pregnancy group. Twin pregnancies are also associated with a greater risk of gestational diabetes [15,16] and, in fact, during pregnancy the administration of hormonal antagonists of insulin, such

Table 3 Associations between gestational diabetes and pre-existing diabetes and pregnancy complications and adverse pregnancy outcomes among deliveries in South Korea, 2010–2012

Complication	2010–2012 Normal group (n = 1 171 575)	Gestational diabetes group (n = 78 716)	Pre-existing diabetes group (n = 32 207)	$P^{\ddagger}$
Pregnancy-induced hypertension without significant proteinuria				
Number of cases (%)	11,669 (1.00)	1,344 (1.71)	957 (2.97)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.73 (1.63–1.83)	3.04 (2.85–3.26)	
Age-adjusted OR (95% CI)	Ref.	1.66 (1.57–1.76)	2.88 (2.69–3.08)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.49 (1.41.1.58)	1.72 (1.60–1.85)	
Pregnancy-induced hypertension with significant proteinuria				
Number of cases (%)	13,218 (1.13)	1,307 (1.66)	1,263 (3.92)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.48 (1.40–1.57)	3.58 (3.37–3.79)	
Age-adjusted OR (95% CI)	Ref.	1.41 (1.33–1.49)	3.33 (3.14–3.53)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.24 (1.17–1.32)	2.00 (1.87–2.13)	
Eclampsia				
Number of cases (%)	605 (0.05)	63 (0.08)	51 (0.16)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.55 (1.20–2.01)	3.07 (2.31–4.09)	
Age-adjusted OR (95% CI)	Ref.	1.48 (1.14–1.92)	2.86 (2.15–3.81)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.28 (0.99–1.66)	1.53 (1.14–2.07)	
Infection of genitourinary tract				
Number of cases (%)	246,378 (21.03)	19,323 (24.55)	8,453 (26.25)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.22 (1.20–1.24)	1.34 (1.30–1.37)	
Age-adjusted OR (95% CI)	Ref.	1.23 (1.21–1.25)	1.35 (1.32–1.38)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.22 (1.20–1.24)	1.32 (1.28–1.35)	
Embolism/deep vein thrombosis				
Number of cases (%)	324 (0.03)	28 (0.04)	40 (0.12)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.29 (0.87–1.89)	4.50 (3.24–6.25)	
Age-adjusted OR (95% CI)	Ref.	1.19 (0.81–1.76)	4.02 (2.89–5.60)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.13 (0.77–1.67)	3.31 (2.35–4.64)	
Puerperal sepsis				
Number of cases (%)	1225 (0.10)	117 (0.15)	39 (0.12)	0.001
Unadjusted OR (95% CI)	Ref.	1.42 (1.18–1.72)	1.16 (0.84–1.59)	
Age-adjusted OR (95% CI)	Ref.	1.46 (1.21–1.77)	1.21 (0.88–1.66)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.46 (1.21–1.76)	1.20 (0.87–1.65)	
Wound infection				
Number of cases (%)	40 732 (3.48)	2129 (2.70)	829 (2.57)	< 0.001
Unadjusted OR (95% CI)	Ref.	0.77 (0.74–0.81)	0.73 (0.69–0.79)	
Age-adjusted OR (95% CI)	Ref.	0.79 (0.75–0.82)	0.76 (0.71–0.81)	
*Multivariate-adjusted OR (95% CI)	Ref.	0.79 (0.76–0.83)	0.76 (0.71–0.82)	
Puerperal sepsis				
Number of cases (%)	1225 (0.10)	117 (0.15)	39 (0.12)	0.001
Unadjusted OR (95% CI)	Ref.	1.42 (1.18–1.72)	1.16 (0.84–1.59)	
Age-adjusted OR (95% CI)	Ref.	1.46 (1.21–1.77)	1.21 (0.88–1.66)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.46 (1.21–1.76)	1.20 (0.87–1.65)	
Antepartum haemorrhage				
Number of cases (%)	27 977 (2.39)	1,805 (2.29)	974 (3.02)	< 0.001
Unadjusted OR (95% CI)	Ref.	0.96 (0.91–1.01)	1.28 (1.20–1.36)	
Age-adjusted OR (95% CI)	Ref.	0.96 (0.91–1.01)	1.27 (1.19–1.36)	
*Multivariate-adjusted OR (95% CI)	Ref.	0.95 (0.90–0.99)	1.24 (1.16–1.32)	
Postpartum haemorrhage				
Number of cases (%)	85 498 (7.30)	5533 (7.03)	1,932 (6.00)	< 0.001
Unadjusted OR (95% CI)	Ref.	0.96 (0.93–0.99)	0.81 (0.77–0.85)	
Age-adjusted OR (95% CI)	Ref.	0.96 (0.93–0.98)	0.81 (0.77–0.84)	
*Multivariate-adjusted OR (95% CI)	Ref.	0.95 (0.93–0.98)	0.80 (0.76–0.83)	
Pelvic and perineal trauma				
Number of cases (%)	68 803 (5.87)	3926 (4.99)	1387 (4.31)	< 0.001
Unadjusted OR (95% CI)	Ref.	0.84 (0.81–0.87)	0.72 (0.68–0.76)	
Age-adjusted OR (95% CI)	Ref.	0.88 (0.85–0.91)	0.77 (0.73–0.82)	
*Multivariate-adjusted OR (95% CI)	Ref.	0.89 (0.86–0.92)	0.79 (0.75–0.84)	
Uterine rupture				
Number of cases (%)	232 (0.02)	25 (0.03)	5 (0.02)	0.062
Unadjusted OR (95% CI)	Ref.	1.60 (1.06–2.42)	0.78 (0.32–1.90)	
Age-adjusted OR (95% CI)	Ref.	1.43 (0.94–2.16)	0.66 (0.27–1.60)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.39 (0.92–2.10)	0.58 (0.24–1.42)	

Table 3 (*Continued*)

Complication	2010–2012 Normal group (n = 1 171 575)	Gestational diabetes group (n = 78 716)	Pre-existing diabetes group (n = 32 207)	$P^{\ddagger}$
Shoulder dystocia				
Number of cases (%)	233 (0.02)	19 (0.02)	13 (0.04)	0.033
Unadjusted OR (95% CI)	Ref.	1.21 (0.76–1.94)	2.03 (1.16–3.55)	
Age-adjusted OR (95% CI)	Ref.	1.17 (0.73–1.86)	1.91 (1.09–3.35)	
†Multivariate-adjusted OR (95% CI)	Ref.	1.23 (0.77–1.97)	2.27 (1.29–3.99)	
Premature separation of placenta				
Number of cases (%)	4888 (0.42)	328 (0.42)	207 (0.64)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.00 (0.89–1.12)	1.54 (1.34–1.78)	
Age-adjusted OR (95% CI)	Ref.	0.97 (0.86–1.08)	1.47 (1.28–1.69)	
*Multivariate-adjusted OR (95% CI)	Ref.	0.94 (0.84–1.05)	1.28 (1.11–1.47)	
Placenta previa				
Number of cases (%)	13 598 (1.16)	1,108 (1.41)	609 (1.89)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.22 (1.14–1.29)	1.64 (1.51–1.78)	
Age-adjusted OR (95% CI)	Ref.	1.10 (1.04–1.18)	1.42 (1.31–1.55)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.10 (1.03–1.17)	1.39 (1.28–1.51)	
Placental disorders				
Number of cases (%)	5584 (0.48)	426 (0.54)	367 (1.14)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.14 (1.03–1.25)	2.41 (2.16–2.68)	
Age-adjusted OR (95% CI)	Ref.	1.07 (0.97–1.19)	2.21 (1.99–2.46)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.02 (0.93–1.13)	1.99 (1.79–2.22)	
Premature rupture of membranes				
Number of cases (%)	234 221 (19.99)	16 388 (20.82)	6820 (21.18)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.05 (1.03–1.07)	1.08 (1.05–1.11)	
Age-adjusted OR (95% CI)	Ref.	1.07 (1.05–1.09)	1.11 (1.08–1.14)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.07 (1.05–1.09)	1.11 (1.08–1.14)	
Preterm delivery				
Number of cases (%)	23 943 (2.04)	2330 (2.96)	1488 (4.62)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.46 (1.40–1.53)	2.32 (2.20–2.45)	
Age-adjusted OR (95% CI)	Ref.	1.40 (1.34–1.46)	2.18 (2.06–2.30)	
†Multivariate-adjusted OR (95% CI)	Ref.	1.29 (1.23–1.34)	1.76 (1.67–1.87)	
Prolonged pregnancy				
Number of cases (%)	10,874 (0.93)	492 (0.63)	228 (0.71)	< 0.001
Unadjusted OR (95% CI)	Ref.	0.67 (0.61–0.74)	0.76 (0.67–0.87)	
Age-adjusted OR (95% CI)	Ref.	0.70 (0.64–0.76)	0.81 (0.71–0.92)	
†Multivariate-adjusted OR (95% CI)	Ref.	0.72 (0.66–0.79)	0.91 (0.79–1.03)	
Liver disorder				
Number of cases (%)	49 265 (4.21)	7455 (9.47)	6220 (19.31)	< 0.001
Unadjusted OR (95% CI)	Ref.	2.38 (2.32–2.45)	5.45 (5.30–5.61)	
Age-adjusted OR (95% CI)	Ref.	2.34 (2.28–2.40)	5.30 (5.15–5.46)	
*Multivariate-adjusted OR (95% CI)	Ref.	2.31 (2.25–2.37)	5.01 (4.87–5.16)	
Chronic renal disease				
Number of cases (%)	2,238 (0.19)	218 (0.28)	458 (1.42)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.45 (1.26–1.67)	7.54 (6.81–8.34)	
Age-adjusted OR (95% CI)	Ref.	1.43 (1.24–1.64)	7.37 (6.65–8.16)	
*Multivariate-adjusted OR (95% CI)	Ref.	1.33 (1.15–1.53)	5.10 (4.58–5.68)	
Acute renal complication				
Number of cases (%)	1,853 (0.16)	127 (0.16)	208 (0.65)	< 0.001
Unadjusted OR (95% CI)	Ref.	1.02 (0.85–1.22)	4.10 (3.55–4.74)	
Age-adjusted OR (95% CI)	Ref.	1.02 (0.85–1.22)	4.07 (3.52–4.70)	
*Multivariate-adjusted OR (95% CI)	Ref.	0.99 (0.83–1.18)	3.53 (3.05–4.10)	

OR, odds ratio; Ref., reference value.
*Adjusted for age, multiple pregnancy, and pre-existing hypertension prior to pregnancy.
†Adjusted for age, multiple pregnancy, pre-existing hypertension prior to pregnancy, and Cesarean section.
‡Chi-squared test.

as human placental lactogen that reduces tissue sensitivity to insulin, results in a diabetogenic state [17]. Additionally, pregnancy-related diabetogenic hormones are higher in a twin pregnancy than in a single pregnancy because of the greater placental mass [18], therefore, a multiple pregnancy is more likely to be affected by gestational diabetes [15,16]. In the present study, the multiple pregnancy rate was greater in the gestational diabetes and pre-existing diabetes groups than in the normal group. Caesarean sections [1,4,8] and pre-existing hypertension [19] are also more commonly associated with gestational diabetes and pre-existing diabetes than with a normal pregnancy. Consistent with this, the present

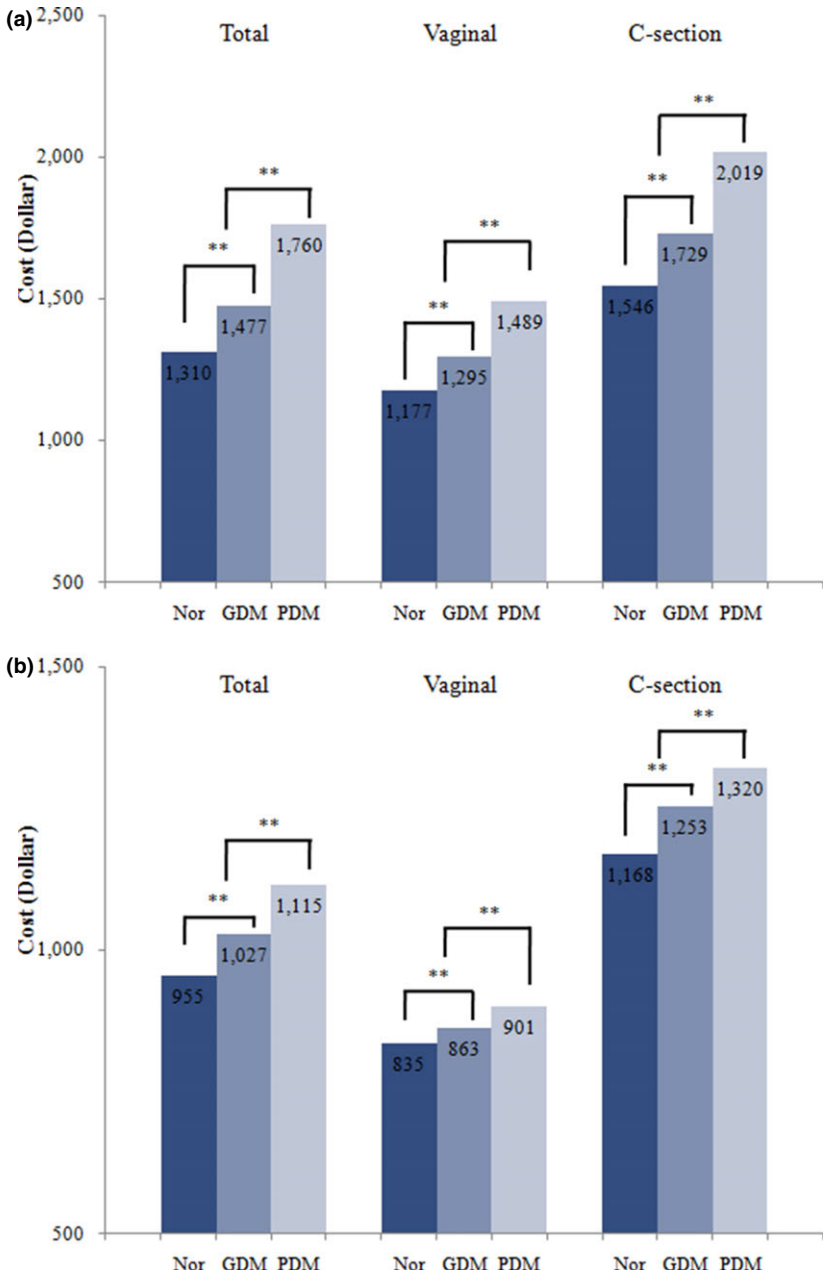

FIGURE 1 (a) Total medical costs during pregnancy in 2010-2012. (b) Delivery costs in 2010-2012. Pair-wise differences among the three groups were evaluated using a Tukey-Kramer multiple comparison. Nor: normal group, GDM: Gestational diabetes mellitus, PDM: Pre-existing diabetes mellitus. ** p-Value <0.05.

study showed that the rates of pre-existing hypertension and Caesarean section were higher in the pre-existing diabetes and gestational diabetes groups relative to the normal group. Maternal age, pre-existing hypertension, the multiple pregnancy rate and the rate of Caesarean section differed among the normal, gestational diabetes and pre-existing diabetes groups. Because we presumed those differences might affect estimations of the influence of pre-existing diabetes or gestational diabetes on pregnancy complications, we used three different models: an unadjusted, an age-adjusted and a multivariate-adjusted model, which was adjusted for maternal age, pre-existing hypertension and multiple pregnancy. In cases of shoulder dystocia, preterm delivery and prolonged pregnancy, Caesarean section was also adjusted for, because those complications could be affected by Caesarean section.

The primary cause of adverse outcomes in subjects with pre-existing diabetes and gestational diabetes is hyperglycaemia, which affects both the mother and the fetus. In fact, several studies have reported a linear relationship between maternal glucose levels and adverse pregnancy outcomes

[20,21]. Based on these findings, adverse pregnancy outcomes might be more prevalent in patients with pre-existing diabetes than in those with gestational diabetes because there is a greater likelihood of elevated glucose levels being present during early pregnancy [14]. In the present study, the influence of pre-existing diabetes or gestational diabetes on pregnancy complications differed based on the type of complication. While the risk of some complications was greater in the pre-existing diabetes group than in the gestational diabetes group, for other complications the risk was lower in the pre-existing diabetes group.

The relationship between pregnancy-induced hypertension and gestational diabetes is controversial [22–24]; several studies have found such an association [22], while others have not [23], and still others suggest that this association varies depending on the type of pregnancy-induced hypertension [24]. These same authors also reported that gestational diabetes increases the risk rates for gestational hypertension, mild pre-eclampsia and severe pre-eclampsia although eclampsia was not related [24]. In the present study, the risk of pregnancy-induced hypertension with or without proteinuria was greater in the gestational diabetes and pre-existing diabetes groups than in the normal pregnancy group, and this risk was greater in the gestational diabetes group than in the pre-existing diabetes group regardless of adjusting. In the case of eclampsia, the risk was greater in both the gestational diabetes and pre-existing diabetes groups than in the normal group, but the risk was not increased in the gestational diabetes group after multivariate adjusting.

The association between venous thromboembolism and gestational diabetes is also controversial; several studies have reported an association between gestational diabetes and venous thromboembolism [25], but this relationship was not found to be significant in other studies [26]. Diabetes during pregnancy is also a known risk factor for urinary tract infections [27], but several studies have reported that gestational diabetes is not associated with this complication [28]. In the present study, both gestational diabetes and pre-existing diabetes were associated with urinary tract infections.

The risks of wound infection, postpartum haemorrhage and pelvic and perineal trauma were lower in the pre-existing diabetes and gestational diabetes groups than in the normal group. This finding may have been influenced by the surgeons' decisions regarding when a delivery should be performed and/or which delivery method would be most appropriate, because a higher rate of planned delivery or Caesarean section in subjects with gestational diabetes or pre-existing diabetes could have decreased the incidence of wound complications or haemorrhage. The risk of shoulder dystocia in this study was greater in the pre-existing diabetes group than in the normal group, but gestational diabetes was not related to this issue. Previous studies have reported that the risk of shoulder dystocia is greater for those with pre-existing diabetes than for those with gestational diabetes [14]. The risks of premature rupture of membranes or preterm delivery were also greater in the pre-existing diabetes and gestational diabetes groups than normal, which corroborates a number of reports of an association between preterm labour and diabetes during pregnancy [1]. Likewise, we identified a higher rate of placenta previa or disorder in the pre-existing diabetes, which confirms previous findings in studies of patients with gestational diabetes and pre-existing diabetes [19]. The risk of a liver disorder and chronic renal disease was also increased in the gestational diabetes and pre-existing diabetes groups in the present study, as was the risk of acute renal complications in the pre-existing diabetes group. Because most complications associated with pre-existing diabetes and gestational diabetes share risk factors such as age, pre-existing hypertension, obesity and multiple pregnancy, it is difficult to determine which factors result in effects that are more harmful during pregnancy in patients with pre-existing diabetes and gestational diabetes; however, the present study identified a trend in which pre-existing diabetes results in more dangerous pregnancy-related complications than gestational diabetes.

In 2007, gestational diabetes increased the total medical cost of a pregnancy in the USA by an average of $3,305 [3]. Similarly, a European study found that total mean healthcare costs adjusted for age, BMI and education were 25.1% higher among females diagnosed with gestational diabetes than among females without gestational diabetes (€6,432 vs €5,143; $P < 0.001$ [29]). The present study also showed that the total costs of pregnancy and delivery were higher for the pre-existing diabetes group than for the gestational diabetes and normal groups. The in-hospital days necessary during delivery in the present study also followed this pattern of significance (pre-existing diabetes > gestational diabetes, pre-existing diabetes > normal and gestational diabetes > normal) and are consistent with a previous study of pregnancy-associated costs [14]. In the present study, the medical costs were estimated using only data from the health insurance claims database that could be confirmed. A more accurate estimation of medical costs should include indirect monetary and non-monetary costs such as increased time off from work or school, psychological stress, and reduced performance by offspring in school [3]. Although the present findings may underestimate the total economic burden associated with gestational diabetes and pre-existing diabetes, the results suggest that gestational diabetes and pre-existing diabetes are important factors that increase medical costs.

The present study had several limitations. First, gestational diabetes or pre-existing diabetes were defined using the ICD-10 codes alone. The screening procedures, diagnosis methods and diagnostic criteria for gestational diabetes and pre-existing diabetes may differ among various hospitals and it is possible that the diagnostic codes for these diseases were missing for some patients. Similarly, the complications were

also defined using the ICD-10 codes, which might have led to the underreporting or misclassification of some complications. It has been suggested that in large population studies the actual strength of association may be overestimated by the calculated odds ratio [14, 30]. Thus, odds ratios, especially in the lower range (e.g. 1–2), should be interpreted with caution as they may not be clinically significant [14, 30]. Another limitation was that obesity, an important risk factor for gestational diabetes and pre-existing diabetes, was not included as a factor because the data were not available. Pregnancy outcomes of patients with pre-existing diabetes and gestational diabetes are related to glucose levels and the diabetes treatment method [20, 21], but this information could not be accessed for the present study.

Strengths of this study include its large sample size. All data were obtained from a national health insurance claims database that contains the information of ~50 million Korean people. Although there is a possibility that the findings of this study are over- or underestimated, they mirror the general trends associated with pre-existing diabetes and gestational diabetes in Korea. These findings may aid in the development of healthcare policies related to pregnant subjects with pre-existing diabetes or gestational diabetes and their babies.

In conclusion, the present study found that pre-existing diabetes and gestational diabetes could result in an increase in the medical costs and complications related to pregnancy.

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Competing interests

None declared.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1 Codes from the International Classification of Diseases 10th version used to classify a delivery.
Table S2 Delivery complications as defined by the International Classification of Diseases 10th version codes.