Obesity Research & Clinical Practice 13 (2019) 156–163

Contents lists available at ScienceDirect

Obesity Research & Clinical Practice

journal homepage: www.elsevier.com/locate/orcp

Original Article

Effects of central obesity on maternal complications in Korean women of reproductive age

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ARTICLE INFO

Article history:
Received 13 January 2019
Received in revised form 3 March 2019
Accepted 11 March 2019

Keywords:
Waist circumference
Central obesity
Maternal complication

ABSTRACT

Background: Considering the obesity-related complications in pregnancy and during delivery, prepregnancy central obesity may also affect pregnancy-related complications. This study aimed to assess the relationship between prepregnancy central obesity and adverse maternal outcomes in Korean women, by using the Korean National Health Insurance Service (NHIS) cohort.
Methods: In this population-based retrospective cohort study, we used data from the NHIS database, which contains information of health-care utilisation, diagnosis and prescription, and mortality for almost the whole Korean population, together with data from the NHIS health checkup database from 2005 to 2015. The NHIS health checkup data (645–280 days before childbirth) of mothers who had deliveries (total, 783,406 deliveries) from 2006 to 2015 were collected. For maternal adverse outcome data, we searched for diagnoses of maternal complications made during the period of 280 days before each delivery. The odds for maternal complications according to 8 body mass index (BMI) and 10 waist circumference (WC) categories were analysed using logistic regression.
Results: The incidence rates of eclampsia/preeclampsia, caesarean section, multiple gestation, and polycystic ovary syndrome (PCOS) increased according to the increase of BMI and WC. In contrast, the incidence rate of premature rupture of membrane (PROM) was inversely correlated with BMI and WC. In the low BMI (<17.5 and 17.5–19.9 kg/m^2) and low WC (<60 and 60.0–64.0 cm) groups, the odds of threatened abortion were elevated.
Conclusion: Prepregnancy WC was closely linked to some maternal complications, including eclampsia/preeclampsia, cesarean section, PCOS, and PROM, in a manner similar to prepregnancy BMI.

Introduction

Obesity is a global health concern. The global prevalence of overweight and obesity in 2014 was 39% and 13%, respectively, according to the report of the World Health Organization (WHO) in 2015. The prevalence of overweight in Korea has also been increasing, from 26.0% in 1998 to 32.4% in 2012 [1].

The prevalence of obesity in women of reproductive age is increasing. In the WHO-Multinational Monitoring of Trends and Determinants in Cardiovascular Disease study, the prevalence of obesity increased significantly in women aged 25–44 years [2]. Also in Korea, the prevalence of overweight increased in 2012 from 1998 in women aged 19–29 and 30–39 years [1].

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https://doi.org/10.1016/j.orcp.2019.03.004
1871-403X/

Obesity during the reproductive age is associated with detrimental obstetric outcomes such as preterm labor, fetal growth restriction, congenital defects, miscarriages, and caesarean section delivery, as well as numerous obstetric complications such as gestational diabetes, preeclampsia, and eclampsia. Moreover, many patients with polycystic ovary syndrome (PCOS) have obesity, and they are more likely to have anovulation and menstrual irregularity, which result in increased use of assisted reproductive technology (ART).

Body fat distribution is closely related to comorbidities of obesity, and central obesity is associated with an increased risk for cardiovascular disease. Waist circumference (WC) is an easily measurable surrogate index of abdominal fatness and a major component in diagnosing metabolic syndrome. Considering the obesity-related complications in pregnancy and during delivery, prepregnancy central obesity may also have an impact on pregnancy-related complications. However, the effect of central obesity on pregnancy has not been widely investigated.

Therefore, we aimed to assess the relationship between prepregnancy central obesity and adverse maternal outcomes in Korean women, by using the Korean NHIS cohort (2005–2015).

Methods

National health insurance system and national health checkup in Korea

The NHIS in Korea is a semi-government organization that serves as the country's health insurance system. In Korea, 97% of the population is enrolled in the Korean NHIS. The NHIS database contains the data of health-care utilisation, diagnosis and prescription, and mortality for almost the whole Korean population.

The NHIS provides regular health checkup to its subscribers. The health checkup is provided annually or biannually, free of charge, to employee subscribers and regional insurance subscribers of all ages, to the subscriber's dependents and household members who are 40 years or older, and to medical aid beneficiary householders who are 19–64 years of age and their household members aged 41–64 years. The NHIS health checkup database contains the data of anthropometric measurements, health screening, and sociodemographic variables.

The NHIS has established the National Health Information Database (NHID), which is a combination of the NHIS database and NHIS health checkup database. The population included in the database was >50 million in 2014. The eligibility database includes information about income-based insurance contributions, demographic variables, and date of death. Additional details about the study methodology and design have been reported previously [3].

Study population

We performed a population-based retrospective cohort study using the NHID from 2005 to 2015. From the NHID, we identified all deliveries from January 1, 2006 to December 31, 2015. For prepregnancy anthropometric measurements, among the mothers who had deliveries, we selected those who underwent an NHIS health checkup from 645 to 280 days before childbirth (N = 783,406). For maternal adverse outcome data, the diagnoses of maternal complications based on the International Classification of Disease 10th revision (ICD-10) that were made during the period of 280 days before each delivery were searched.

Among all women who delivered during the study period, we selected those aged ≥18 years but ≤45 years, and underwent health checkups as employee subscribers. We excluded those who were regional insurance subscribers (n = 34,193), those were <18 or >46 years old (n = 76), and those with missing data (n = 145). For multiple deliveries from the same mother, we included those awaiting first delivery (19,900 deliveries were excluded). Finally, we analysed 729,092 deliveries in this study. The WC measurement was started in 2009, and the analysis including WC data was performed in 492,633 deliveries.

This study was approved by the Institutional Review Board of the Korea National Institute for Bioethics Policy (P01-201603-21-005) and had permission from the NHIS to use the health checkup data (NHIS-2018-4–042). De-identified and anonymised data were used for analyses.

Prepregnancy data of anthropometric measurements, sociodemographic variables, and chronic diseases

BMI (kg/m^2) was calculated as weight (kg) divided by the square of height (m). WC was measured and expressed in centimeters. We divided the prepregnancy BMI into 8 categories, as follows: <17.5, 17.5–19.9, 20.0–22.4, 22.5–24.9, 25.0–27.4, 27.5–29.9, 30.0–32.4, and ≥32.5 kg/m^2. We also divided the prepregnancy BMI into 6 categories according to standard classifications as a supplement, although for BMI cut-off of morbid obesity, we used 33 kg/m^2 instead 35 kg/m^2, because the number of mothers with BMI over 35 and complications was too small to analyse in this population. The prepregnancy WC was categorised into 10 groups, as follows: <60, 60.0–64.9, 65.0–69.9, 70.0–74.9, 75.0–79.9, 80.0–84.9, 85.0–89.9, 90.0–94.9, 95.0–99.9, and ≥100 cm.

General health behaviors were gathered using self-questionnaires. Subjects with smoking histories were categorised as non-smoker, ex-smoker, or current smoker. Alcohol drinking was categorised by frequency into 0, 1–2, or ≥3 times/week. Regular exercise, defined as vigorous physical activity for at least 20 min/day, was categorised by frequency into 0, 1–4, and ≥5 times/week.

Diabetes was defined as a fasting plasma glucose level of ≥126 mg/dL (from the NHIS health checkup) or at least 1 claim per year for an antidiabetic medication prescription under ICD-10 codes E11–14. Hypertension was defined as systolic blood pressure/diastolic blood pressure ≥140/90 mmHg or at least 1 claim per year for an antihypertensive medication prescription under ICD-10 codes I10–I15. Dyslipidemia was defined as a total cholesterol level of ≥240 mg/dL or at least 1 claim per year for an antihyperlipidemic medication prescription under ICD-10 code E78.

Adverse maternal outcomes

Adverse maternal outcomes (identified by ICD codes) within 280 days of the deliveries were assessed. Eclampsia/preeclampsia, threatened abortion, cesarean section, premature rupture of membrane (PROM), and PCOS were defined as at least 1 claim per year. Multiple gestation including twin, triplet and higher order pregnancies, was defined as at least 1 claim per year under O84 code (O84.0; Multiple delivery, all spontaneous, O84.1; Multiple delivery, all by forceps and vacuum extractor, O84.2; Multiple delivery, all by caesarean section, O84.8; Other multiple delivery, O84.9; Multiple delivery, unspecified) without female infertility (N97).

Statistical analysis

The general characteristics of subjects are expressed as means ± standard deviation for continuous variables and number (%) for categorical variables. The prepregnancy characteristics and maternal complications were compared between 2 age groups: age <35 and ≥35 years. The odds ratios (ORs) and 95% confidence intervals (CIs) for eclampsia/preeclampsia, threatened abortion, cesarean section, PROM, multiple gestation, and PCOS according to

Table 1
Prepregnancycharacteristics of the participants.

Characteristics		Data
Age (year)		29.84 ± 3.56
BMI (kg/m^2)		21.01 ± 2.82
Blood pressure (mmHg)	Systolic	110.12 ± 10.83
	Diastolic	69.25 ± 8.08
Glucose (mg/dL)		87.56 ± 11.18
Total cholesterol (mg/dL)		176.14 ± 30.06
BMI (kg/m^2)		
	<17.5	39,874 (5.47)
	17.5–19.9	258,541 (35.46)
	20.0–22.4	261,275 (35.84)
	22.5–24.9	107,924 (14.8)
	25.0–27.4	38,474 (5.28)
	27.5–29.9	14,285 (1.96)
	30.0–32.4	5749 (0.79)
	≥32.5	2970 (0.41)
WC (cm)		
	<60	15,872 (3.22)
	60.0–64.9	88,143 (17.89)
	65.0–69.9	152,343 (30.92)
	70.0–74.9	120,176 (24.39)
	75.0–79.9	61,593 (12.5)
	80.0–84.9	30,785 (6.25)
	85.0–89.9	13,111 (2.66)
	90.0–94.9	6071 (1.23)
	95.0–99.9	2628 (0.53)
	≥100	1911 (0.39)
Smoking		19,734 (2.73)
Alcohol drinking		453,297 (62.65)
Exercise		238,425 (48.58)
Hypertension		10,547 (1.45)
Diabetes		4646 (0.64)
Dyslipidemia		22,383 (3.07)

N = 729 092.
Data are expressed as mean ± standard deviation or number (%).
BMI: body mass index, WC: waist circumference.

the 8 BMI categories were analysed using logistic regression models, with the BMI of 20.0–22.4 kg/m^2 as a reference after adjusting for age, smoking, and hypertension in model 2, and age, smoking, hypertension, diabetes, dyslipidemia, alcohol drinking, and exercise in model 3. The ORs and 95% CIs according to the 10 WC categories were analysed using the WC of 70.0–74.9 cm as a reference, in the same manner. All statistical analyses were conducted using SAS version 9.3 (SAS Institute, Cary, NC, USA), and all 2-tailed $p < 0.05$ was considered statistically significant.

Results

Prepregnancy characteristics of the study population

The prepregnancy characteristics are presented in Table 1 and Supplementary Table S1. For prepregnancy BMI, large proportions of the population were categorised into the 17.5–19.9 kg/m^2 (35.46%) and 20.0–22.4 kg/m^2 (35.84%) groups. For prepregnancy WC, the 2 largest groups were the 65.0–69.9 cm (30.92%) and 70.0–74.9 cm (24.39%) groups. Of the women, <3% smoked and >63% drank alcohol. The prevalence of preexisting hypertension, diabetes, and dyslipidemia was low in this population. The prevalence rate of dyslipidemia was around 3%, which was the highest among the 3 conditions. The prevalence rates of all 3 conditions were higher in the older group ($p < 0.01$).

Maternal complications

The incidence of maternal complications is listed in Table 2 and Supplementary Table S2. Except for PCOS ($p = 0.19$), the incidence rates of eclampsia/preeclampsia ($p < 0.01$), threatened abortion ($p < 0.01$), cesarean section ($p < 0.01$), PROM ($p = 0.01$), and multiple gestation ($p < 0.01$) were higher in the older group.

Table 2
Incidence of maternal complications.

Eclampsia/preeclampsia	9083 (1.25)
Threatened abortion	98,891 (13.56)
Cesarean section	243,548 (33.4)
Premature rupture of membrane	103,899 (14.25)
Multiple gestation	12,176 (1.67)
Polycystic ovary syndrome	1899 (0.26)

Data are expressed as number (%).

The ORs and 95% CIs of maternal complications according to BMI groups are presented in Table 3 and Fig. 1A. Table 4 and Fig. 1B shows the ORs and 95% CIs of maternal complications according to WC groups. The ORs and 95% CIs of maternal complications according to standard BMI categories are presented in Supplementary Table S3. The incidence rates of eclampsia/preeclampsia, caesarean section, multiple gestation, and PCOS increased in the obese groups. The incidence rates of eclampsia/preeclampsia, caesarean section, multiple gestation, and PCOS increased according to the increase of BMI. Furthermore, the incidence rates of these complications were positively correlated with the increase of WC. On the contrary, the incidence rate of PROM was inversely correlated with BMI and WC.

The relationship between the anthropometric measurements and the incidence rate of threatened abortion was different from those of the above-mentioned complications. The incidence rate of threatened abortion was stable in mothers with normal weight and those with obesity. However, in the low BMI (<17.5 and 17.5–19.9 kg/m^2) and low WC (<60 and 60.0–64.0 cm) groups, the odds of threatened abortion were elevated.

Discussion

In this study, we observed that prepregnancy central obesity is closely linked to some maternal complications, including eclampsia/preeclampsia, caesarean section, PROM, and PCOS. We also found that threatened abortion occurs more frequently in mothers whose WCs were low before pregnancy than in those whose prepregnancy WCs were normal or high. The event rate of multiple gestation was significantly low in mothers with low prepregnancy WC.

Some large epidemiologic studies have investigated the relationship between prepregnancy BMI and adverse obstetric outcomes, and these studies indicated that prepregnancy obesity increases the risks of preeclampsia, gestational diabetes, and caesarean section in various parts of the world [4–6]. Our analysis reconfirmed that the risks of eclampsia/preeclampsia and caesarean section were elevated in the high BMI groups in this large Korean cohort. Our results showed that high prepregnancy BMI was also related to an increased risk of multiple gestation. For threatened abortion, the risk was significantly increased in the low BMI group, but was not definite in the high BMI group.

Both extremely low BMI and extremely low WC were related to an increased risk of threatened abortion. Threatened abortion is defined as uterine bleeding in the early period of pregnancy, especially the first trimester, and is known to be related to increased risks of adverse obstetric outcomes [7]. A substantial number of patients with threatened abortion miscarry [8]. However, besides embryonic or fetal chromosomal abnormalities, the risk factors of threatened abortion are not well understood, and to the best of our knowledge, prepregnancy maternal body weight has not been investigated as a risk factor of threatened abortion. In this study, the BMI 22.5–24.9 kg/m^2 group and the WC 75.0–79.9 cm group showed the lowest incidence rate of threatened abortion.

Table 3
Odds ratios and 95% confidence intervals for maternal complications according to prepregnancy body mass index.

	Body mass index (kg/m^2)							
	<17.5	17.5–19.9	20.0–22.4	22.5–24.9	25.0–27.4	27.5–29.9	30.0–32.4	≥32.5
n	39,874	258,541	261,275	107,924	38,474	14,285	5749	2970
Eclampsia/preeclampsia								
n (%)	284 (0.71)	2271 (0.88)	3034 (1.16)	1736 (1.61)	881 (2.29)	467 (3.27)	222 (3.86)	188 (6.33)
Model 1	0.611 (0.540, 0.690)	0.754 (0.714, 0.797)	1	1.392 (1.311, 1.477)	1.995 (1.849, 2.152)	2.877 (2.606, 3.176)	3.419 (2.976, 3.928)	5.758 (4.946, 6.702)
Model 2	0.627 (0.554, 0.709)	0.771 (0.730, 0.815)	1	1.334 (1.256, 1.417)	1.759 (1.628, 1.900)	2.283 (2.061, 2.529)	2.358 (2.040, 2.727)	3.401 (2.898, 3.991)
Model 3	0.623 (0.530, 0.732)	0.773 (0.720, 0.830)	1	1.346 (1.247, 1.452)	1.698 (1.540, 1.871)	2.118 (1.864, 2.406)	2.138 (1.790, 2.553)	2.917 (2.406, 3.537)
Threatened abortion								
n (%)	5788 (14.52)	35,786 (13.84)	34,865 (13.34)	14,175 (13.13)	5073 (13.19)	1962 (13.73)	813 (14.14)	429 (14.44)
Model 1	1.103 (1.070, 1.136)	1.043 (1.027, 1.060)	1	0.982 (0.962, 1.003)	0.986 (0.956, 1.018)	1.034 (0.985, 1.086)	1.07 (0.992, 1.153)	1.096 (0.989, 1.215)
Model 2	1.109 (1.076, 1.143)	1.047 (1.030, 1.064)	1	0.977 (0.957, 0.998)	0.977 (0.947, 1.009)	1.023 (0.974, 1.074)	1.05 (0.973, 1.132)	1.076 (0.970, 1.193)
Model 3	1.108 (1.067, 1.151)	1.045 (1.025, 1.066)	1	0.996 (0.971, 1.022)	0.989 (0.952, 1.028)	1.063 (1.003, 1.126)	1.093 (1.001, 1.192)	1.179 (1.051, 1.322)
Cesarean section								
n (%)	9739 (24.42)	73,251 (28.33)	87,449 (33.47)	43,291 (40.11)	17,456 (45.37)	7412 (51.89)	3131 (54.46)	1819 (61.25)
Model 1	0.643 (0.627, 0.658)	0.786 (0.777, 0.795)	1	1.331 (1.312, 1.351)	1.651 (1.616, 1.687)	2.143 (2.072, 2.217)	2.376 (2.255, 2.505)	3.137 (2.912, 3.379)
Model 2	0.678 (0.661, 0.694)	0.810 (0.800, 0.820)	1	1.290 (1.271, 1.310)	1.568 (1.534, 1.603)	2.003 (1.936, 2.073)	2.207 (2.092, 2.328)	2.855 (2.648, 3.079)
Model 3	0.688 (0.668, 0.709)	0.811 (0.800, 0.823)	1	1.287 (1.265, 1.311)	1.547 (1.507, 1.587)	1.953 (1.876, 2.034)	2.175 (2.045, 2.314)	2.691 (2.472, 2.930)
Premature rupture of membrane								
n (%)	5876 (14.74)	38,583 (14.92)	37,074 (14.19)	14,508 (13.44)	4954 (12.88)	1794 (12.56)	731 (12.72)	379 (12.76)
Model 1	1.045 (1.015, 1.077)	1.061 (1.045, 1.077)	1	0.939 (0.920, 0.959)	0.894 (0.866, 0.923)	0.869 (0.826, 0.914)	0.881 (0.815, 0.953)	0.885 (0.794, 0.986)
Model 2	1.067 (1.036, 1.100)	1.072 (1.056, 1.089)	1	0.929 (0.909, 0.948)	0.880 (0.852, 0.909)	0.855 (0.813, 0.900)	0.873 (0.807, 0.944)	0.882 (0.791, 0.984)
Model 3	1.081 (1.048, 1.116)	1.076 (1.058, 1.093)	1	0.920 (0.900, 0.940)	0.840 (0.813, 0.868)	0.793 (0.753, 0.836)	0.776 (0.716, 0.842)	0.747 (0.668, 0.834)
Multiple gestation								
n (%)	530 (1.33)	3982 (1.54)	4563 (1.75)	1937 (1.79)	674 (1.75)	281 (1.97)	127 (2.21)	82 (2.76)
Model 1	0.758 (0.692, 0.830)	0.880 (0.843, 0.919)	1	1.028 (0.974, 1.085)	1.003 (0.925, 1.088)	1.129 (1.000, 1.275)	1.271 (1.063, 1.519)	1.597 (1.280, 1.993)
Model 2	0.836 (0.763, 0.916)	0.927 (0.888, 0.968)	1	0.979 (0.928, 1.033)	0.928 (0.855, 1.008)	1.037 (0.917, 1.173)	1.182 (0.988, 1.415)	1.506 (1.204, 1.883)
Model 3	0.850 (0.764, 0.946)	0.927 (0.881, 0.975)	1	0.979 (0.920, 1.043)	0.945 (0.861, 1.038)	1.043 (0.908, 1.198)	1.163 (0.951, 1.421)	1.472 (1.153, 1.881)
Polycystic ovary syndrome								
n (%)	92 (0.23)	538 (0.21)	665 (0.25)	310 (0.29)	149 (0.39)	78 (0.55)	37 (0.64)	30 (1.01)
Model 1	0.906 (0.729, 1.127)	0.817 (0.729, 0.916)	1	1.129 (0.986, 1.292)	1.524 (1.275, 1.820)	2.152 (1.701, 2.722)	2.539 (1.821, 3.538)	4.000 (2.769, 5.776)
Model 2	0.909 (0.730, 1.132)	0.821 (0.732, 0.920)	1	1.131 (0.988, 1.295)	1.509 (1.261, 1.806)	2.150 (1.697, 2.724)	2.512 (1.798, 3.509)	3.884 (2.676, 5.639)
Model 3	0.953 (0.740, 1.228)	0.828 (0.725, 0.946)	1	1.141 (0.976, 1.334)	1.447 (1.177, 1.779)	2.023 (1.547, 2.645)	2.537 (1.780, 3.615)	3.535 (2.366, 5.281)

Model 1: crude.
Model 2: adjusted by age, smoking and hypertension.
Model 3: adjusted by age, smoking, hypertension, diabetes, dyslipidemia, alcohol drinking and exercise.

Table 4
Odds ratios and 95% confidence intervals for maternal complications according to prepregnancy waist circumference.

	Waist circumference (cm)									
	<60.0	60.0–64.9	65.0–69.9	70.0–74.9	75.0–79.9	80.0–84.9	85.0–89.9	90.0–94.9	95.0–99.9	≥100
n	15,872	88,143	152,343	120,176	61,593	30,785	13,111	6071	2628	1911
Eclampsia/preeclampsia										
n (%)	109 (0.69)	710 (0.81)	1369 (0.9)	1428 (1.19)	828 (1.34)	524 (1.7)	272 (2.07)	188 (3.1)	92 (3.5)	83 (4.34)
Model 1	0.575 (0.473, 0.699)	0.675 (0.617, 0.739)	0.754 (0.700, 0.812)	1	1.133 (1.040, 1.235)	1.440 (1.302, 1.593)	1.762 (1.546, 2.008)	2.657 (2.277, 3.101)	3.017 (2.434, 3.738)	3.776 (3.012, 4.734)
Model 2	0.610 (0.501, 0.743)	0.713 (0.651, 0.780)	0.779 (0.723, 0.840)	1	1.084 (0.994, 1.182)	1.285 (1.160, 1.423)	1.451 (1.269, 1.658)	2.015 (1.720, 2.361)	2.020 (1.619, 2.520)	2.280 (1.802, 2.884)
Model 3	0.615 (0.505, 0.750)	0.720 (0.657, 0.788)	0.785 (0.728, 0.846)	1	1.073 (0.983, 1.170)	1.262 (1.139, 1.399)	1.385 (1.211, 1.584)	1.833 (1.56, 2.154)	1.775 (1.415, 2.225)	1.923 (1.510, 2.449)
Threatened abortion										
n (%)	2162 (13.62)	11,848 (13.44)	19,952 (13.1)	15,735 (13.09)	7949 (12.91)	4095 (13.3)	1755 (13.39)	837 (13.79)	369 (14.04)	276 (14.44)
Model 1	1.047 (0.997, 1.099)	1.031 (1.005, 1.057)	1.000 (0.978, 1.023)	1	0.984 (0.956, 1.012)	1.018 (0.981, 1.057)	1.026 (0.973, 1.082)	1.061 (0.985, 1.144)	1.084 (0.970, 1.212)	1.120 (0.985, 1.274)
Model 2	1.062 (1.011, 1.114)	1.042 (1.016, 1.069)	1.006 (0.984, 1.029)	1	0.977 (0.949, 1.006)	1.008 (0.972, 1.046)	1.012 (0.960, 1.068)	1.043 (0.968, 1.125)	1.067 (0.954, 1.193)	1.099 (0.966, 1.250)
Model 3	1.064 (1.013, 1.117)	1.043 (1.016, 1.070)	1.008 (0.986, 1.031)	1	0.978 (0.950, 1.007)	1.009 (0.972, 1.047)	1.014 (0.962, 1.070)	1.045 (0.969, 1.127)	1.069 (0.955, 1.195)	1.098 (0.964, 1.251)
Cesarean section										
n (%)	4429 (27.9)	25,801 (29.27)	48,587 (31.89)	42,002 (34.95)	23,595 (38.31)	12,906 (41.92)	6000 (45.76)	2983 (49.14)	1338 (50.91)	1054 (55.15)
Model 1	0.720 (0.694, 0.747)	0.770 (0.756, 0.785)	0.872 (0.858, 0.886)	1	1.156 (1.133, 1.179)	1.344 (1.310, 1.378)	1.570 (1.514, 1.629)	1.798 (1.707, 1.893)	1.930 (1.787, 2.086)	2.288 (2.089, 2.506)
Model 2	0.778 (0.750, 0.808)	0.812 (0.797, 0.827)	0.896 (0.882, 0.911)	1	1.127 (1.104, 1.150)	1.283 (1.251, 1.317)	1.479 (1.426, 1.535)	1.680 (1.594, 1.770)	1.785 (1.651, 1.931)	2.089 (1.905, 2.290)
Model 3	0.783 (0.754, 0.812)	0.814 (0.799, 0.830)	0.897 (0.882, 0.911)	1	1.125 (1.103, 1.148)	1.276 (1.244, 1.310)	1.467 (1.414, 1.522)	1.651 (1.567, 1.740)	1.761 (1.628, 1.905)	2.049 (1.867, 2.248)
Premature rupture of membrane										
n (%)	3809 (24)	20,018 (22.71)	33,141 (21.75)	24,723 (20.57)	12,155 (19.73)	5851 (19.01)	2376 (18.12)	1077 (17.74)	425 (16.17)	324 (16.95)
Model 1	1.219 (1.172, 1.268)	1.134 (1.111, 1.159)	1.073 (1.054, 1.094)	1	0.949 (0.926, 0.973)	0.906 (0.878, 0.935)	0.855 (0.816, 0.895)	0.833 (0.778, 0.891)	0.745 (0.671, 0.827)	0.788 (0.699, 0.889)
Model 2	1.196 (1.150, 1.243)	1.121 (1.097, 1.145)	1.067 (1.047, 1.087)	1	0.955 (0.932, 0.979)	0.917 (0.888, 0.947)	0.867 (0.828, 0.909)	0.845 (0.790, 0.904)	0.761 (0.685, 0.845)	0.808 (0.716, 0.911)
Model 3	1.204 (1.158, 1.253)	1.126 (1.102, 1.150)	1.069 (1.049, 1.089)	1	0.955 (0.932, 0.978)	0.916 (0.887, 0.946)	0.867 (0.827, 0.908)	0.849 (0.793, 0.908)	0.767 (0.691, 0.853)	0.826 (0.731, 0.932)
Multiple gestation										
n (%)	212 (1.34)	1368 (1.55)	2660 (1.75)	2365 (1.97)	1235 (2.01)	657 (2.13)	272 (2.07)	108 (1.78)	64 (2.44)	47 (2.46)
Model 1	0.675 (0.586, 0.778)	0.785 (0.734, 0.840)	0.885 (0.837, 0.936)	1	1.019 (0.951, 1.093)	1.086 (0.996, 1.186)	1.055 (0.930, 1.198)	0.902 (0.743, 1.096)	1.245 (0.968, 1.600)	1.257 (0.939, 1.684)
Model 2	0.769 (0.667, 0.886)	0.855 (0.799, 0.915)	0.926 (0.875, 0.979)	1	0.982 (0.916, 1.053)	1.027 (0.941, 1.121)	0.987 (0.868, 1.121)	0.841 (0.692, 1.024)	1.179 (0.915, 1.520)	1.211 (0.903, 1.624)
Model 3	0.771 (0.669, 0.890)	0.858 (0.802, 0.918)	0.928 (0.877, 0.981)	1	0.984 (0.918, 1.056)	1.033 (0.946, 1.128)	0.984 (0.866, 1.119)	0.840 (0.690, 1.022)	1.172 (0.908, 1.512)	1.212 (0.903, 1.628)
Polycystic ovary syndrome										
n (%)	34 (0.21)	229 (0.26)	373 (0.24)	343 (0.29)	202 (0.33)	117 (0.38)	60 (0.46)	38 (0.63)	17 (0.65)	19 (0.99)
Model 1	0.750 (0.527, 1.067)	0.910 (0.770, 1.076)	0.857 (0.740, 0.993)	1	1.150 (0.966, 1.368)	1.333 (1.080, 1.645)	1.606 (1.220, 2.114)	2.201 (1.572, 3.080)	2.275 (1.396, 3.708)	3.508 (2.206, 5.581)
Model 2	0.737 (0.517, 1.049)	0.897 (0.758, 1.061)	0.851 (0.734, 0.986)	1	1.158 (0.973, 1.380)	1.357 (1.099, 1.675)	1.634 (1.241, 2.153)	2.233 (1.593, 3.128)	2.295 (1.406, 3.747)	3.521 (2.207, 5.618)
Model 3	0.751 (0.527, 1.070)	0.902 (0.762, 1.068)	0.852 (0.735, 0.988)	1	1.142 (0.958, 1.360)	1.317 (1.066, 1.627)	1.506 (1.139, 1.990)	1.976 (1.406, 2.778)	1.960 (1.196, 3.213)	2.841 (1.766, 4.571)

Model 1: crude.
Model 2: adjusted by age, smoking and hypertension.
Model 3: adjusted by age, smoking, hypertension, diabetes, dyslipidemia, alcohol drinking and exercise.

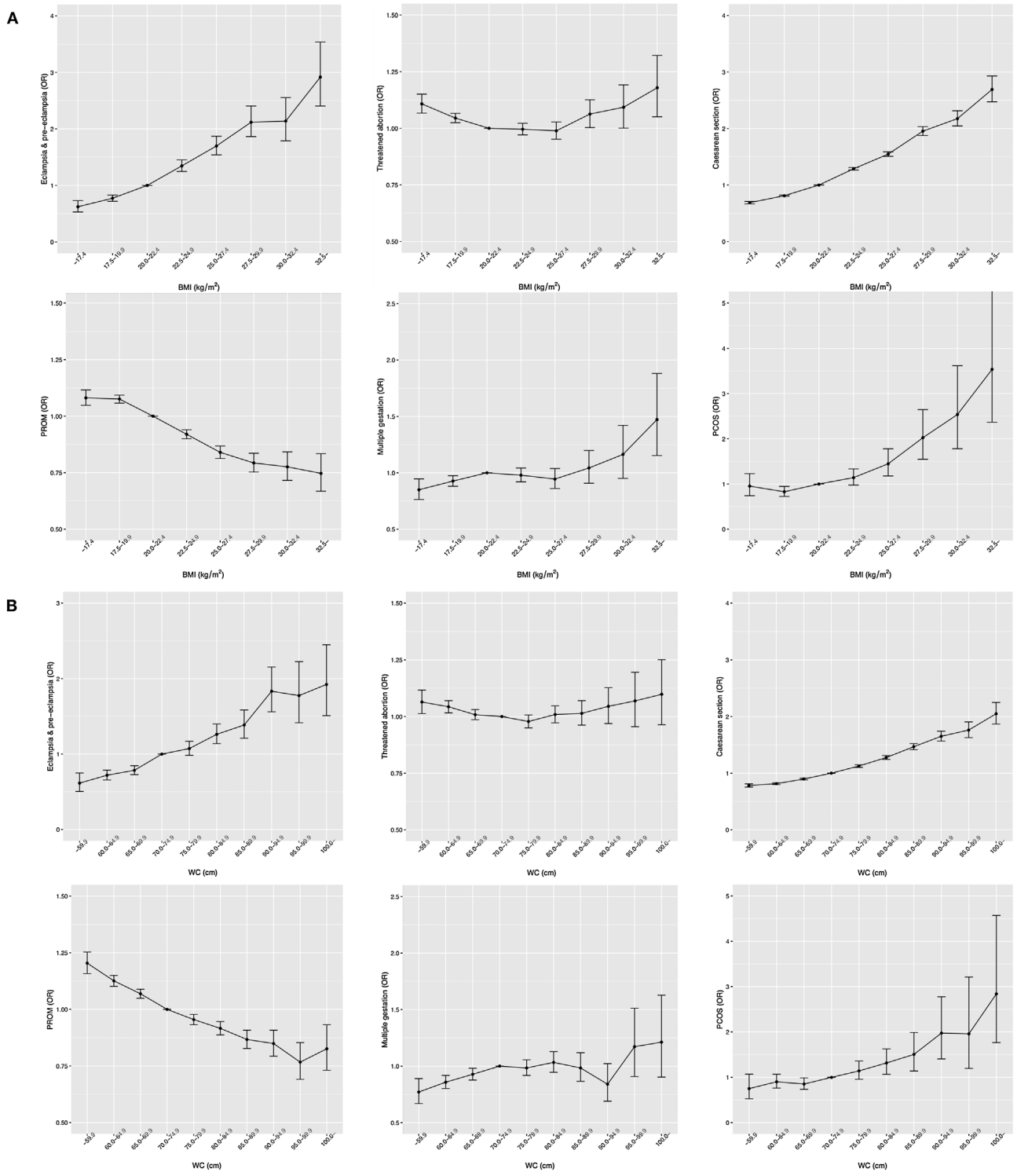

Fig. 1. Odds ratios and 95% confidence intervals for each of maternal complications according to prepregnancy body mass index and waist circumference. (A) For maternal BMI, and (B) for waist circumference.

On the contrary, the underweight groups with BMI < 17.5 kg/m^2 and WC < 60.0 cm showed the highest incidence rate. There is a report suggesting that sex hormone alteration can be a mechanism of threatened abortion [9]. Underweight mothers might have an altered sex hormone status that can lead to more frequent unstable early pregnancy status and uterine bleeding.

There was an inverse relationship between prepregnancy BMI/WC and the risk of PROM in this study. Previously, some research groups reported that high BMI before pregnancy was linked with an increased risk of preterm PROM in several populations [10–12]. On the contrary, the rate of spontaneous preterm birth, a large part of which is preterm PROM, was lower in mothers with prepregnancy obesity in other studies [13,14]. Some explanations can be suggested for the relationship between maternal body weight and preterm PROM or preterm birth. The suspected mechanisms of the increased risk of preterm PROM or preterm

birth in mothers with prepregnancy obesity are obesity-induced inflammation [15] and the adverse influences of obesity on placental pathology [16]. The increased risk of preterm PROM or preterm birth in mothers who were lean before pregnancy can be explained in the aspect of nutrition. The maternal BMI reflects the nutritional status very well, and women with low BMI are considered to have an increased risk of preterm birth, which is partially mediated by a low plasma volume and micronutrient deficiencies [17]. This discrepancy can be explained by 2 reasons. One reason is the heterogeneity of PROM. PROM is composed of term PROM and preterm PROM. Although membrane rupture at term can be a normal physiologic process and is followed by the prompt onset of spontaneous labor, preterm PROM may result from a variety of pathologic mechanisms and can result in fetal complications of prematurity and maternal complications of intrauterine infection. In this study, however, both term and preterm PROM were considered and analysed as a single complication. The other reason is the study population. The risk of preterm birth differ among different ethnicities, and preterm birth occurs substantially frequently in African Americans [18]. This study was conducted in Korean women, and the different ethnicity could have caused the disparity.

Multiple gestation more commonly occurred in mothers with high BMI before pregnancy, whereas the relationship between high WC before pregnancy and increased risk of multiple gestation was not significant. In Korea, the diagnosis of female infertility is essential in receiving financial support for ART. Multiple gestation (ICD-10 code O84) in female infertility (ICD-10 code N97) means multiple gestation from ART in infertility mothers. By excluding multiple gestations from ART, we analysed only naturally conceived multiple gestations, and attempted to show the relationship between obesity and multiple gestation. Two hormones, follicle-stimulating hormone (FSH) and insulin-like growth factor (IGF), seem to play a crucial role in the association between maternal excess adiposity and increased incidence of multiple gestation. First, a high FSH level is clearly associated with spontaneous dizygotic twinning [19]. The increase in FSH level induces excess body fat accumulation and decreased thermogenesis [20]. A study on the effect of obesity on the 24-h mean serum FSH level in healthy, weight-stable, regularly cycling, premenopausal women with BMI ranging from 20 to 94 kg/m^2 reported that there was a positive correlation between serum FSH levels and BMI [21]. Second, an elevated level of IGF, which enhances ovarian follicle recruitment and decreases ovum apoptosis, might be linked to a high twinning rate in obese mothers [22]. The relationship between IGF-1 and obesity is not simple. According to a study with data from the Third National Health and Nutrition Examination Survey [23], the IGF-1 level does not linearly decrease with increasing BMI, whereas the mean IGF-1 level decreases with increasing WC. IGF-1 level seems more closely related to central adiposity than to total adiposity. The low IGF-1 level in mothers with a high WC may be a reason for the lack of a significant increase in multiple gestations in our study.

In this study, the rate of pregnancy with PCOS was 0.26% of all pregnancies, and both prepregnancy obesity and central obesity were linked with the increase of pregnancies with PCOS. The population-based prevalence of PCOS ranged from 6% to 10% of all reproductive-age women [24]. In Korea, Rotterdam criteria, which required two out of three, i.e. (1) oligo- or anovulation, (2) clinical and/or biochemical signs of hyperandrogenism, (3) polycystic ovaries (by ultrasound), is commonly applied for the diagnosis of PCOS in clinical situation, with exclusion of other androgen excess disorders. Because PCOS is usually diagnosed before or in the early stage of pregnancy, it is different from other maternal complications that occur during the period of pregnancy. Although the relationship between obesity and PCOS has been described well [25], pregnancy in women with both PCOS and obesity has not been vividly reported. Our data show that the odds of pregnancy with PCOS increase in women with prepregnancy obesity and central obesity.

WC has not been thoroughly assessed in the field of obstetrics. Recently, a research group reported that WC measured at 4–12 weeks' gestation was related to the risk of gestational diabetes mellitus in Chinese women [26]. Increased abdominal subcutaneous fat thickness measured using ultrasonography in the first and second trimesters was reported by Australian researchers to be a predictor of pregnancy-related maternal complications [27,28]. However, in these 3 previous studies, measurements were taken in the middle of pregnancy. Because weight reduction is not recommended during pregnancy, measurements of WC and abdominal subcutaneous fat thickness during pregnancy have less clinical significance than prepregnancy WC measurements.

A considerable number of previous studies have examined the relationship between prepregnancy maternal body weight and adverse pregnancy outcomes. Compared with previous studies in this field, our study has 2 strengths. First, the database used in this study is very large and nationally representative. The NHID is the Korean national representative health-care database containing screening health checkup data and disease diagnosis and treatment data of almost all Korean adults. We analysed >700,000 pregnancies in Korean women who underwent general health checkups before conception. Second, the prepregnancy maternal anthropometric indices and health status of the participants were accurate. In many previous studies that investigated the relationship between prepregnancy BMI and adverse obstetric outcomes, the prepregnancy weight and height were based on maternal self-report or assessment at the first antenatal visit. There are significant differences between self-reported prepregnancy weight versus measured weight [29]. However, in our study, prepregnancy anthropometric and health status data were based on real measurements in the period of 1 year before conception.

Our data demonstrated 2 new insights on the adverse effects of maternal obesity on pregnancy. One is the relationship between central obesity and maternal adverse pregnancy outcomes, and the other is the relationship between prepregnancy obesity and the risks of threatened abortion or multiple gestation. To the best of our knowledge, these relationships have not been thoroughly investigated previously. There are two limitations in this study. One is that we included women with prepregnancy data only, with missing data of post-delivery anthropometric indices and change of gestational weight/WC. The other is that there is no data for mothers' histories of taking corticosteroids or thyroid drugs, which are associated with both of patient's body weights and maternal complication. The drug histories in the period of pregnancy or before conception are potential confounding factors for the association.

This study suggests that maintaining proper body weight and WC before conception is effective for reducing maternal complications. Both extremely high and extremely low BMI/WC negatively affect pregnancy. However, it is difficult to suggest the appropriate range of prepregnancy BMI or WC because of the linear increase of maternal risks according to the prepregnancy BMI/WC.

In conclusion, prepregnancy WC is closely linked to some maternal complications, including eclampsia/preeclampsia, caesarean section, PCOS, and PROM, in a similar manner as prepregnancy BMI. Threatened abortion occurs more frequently in mothers with low prepregnancy WC than in those with normal or high prepregnancy WC. The event rate of multiple gestation was significantly low in mothers with low prepregnancy WC.

Funding

This work was partially supported by the Korean Society for the Study of Obesity.

Conflicts of interest

The authors have nothing to declare.

Ethical statement

We performed a population-based retrospective cohort study using the Korean National Health Information Database (NHID), which is a combination of the Korean National Health Insurance Service (NHIS) database and NHIS health checkup database.

This study was approved by the Institutional Review Board of the Korea National Institute for Bioethics Policy (P01-201603-21-005) and had permission from the NHIS to use the health checkup data (NHIS-2018-4-042). De-identified and anonymised data were used for analyses.

CRediT authorship contribution statement

Jisun Lim: Methodology, Writing - original draft. **Kyungdo Han:** Methodology, Software, Validation. **Suk Young Kim:** Supervision. **Young Hye Cho:** Writing - original draft. **Yeong Sook Yoon:** Writing - original draft. **Hye Soon Park:** Supervision. **Soon Jib Yoo:** Project administration, Funding acquisition. **Kyoung Kon Kim:** Conceptualization, Methodology, Writing - original draft.

Acknowledgements

We thank the Korean National Health Insurance Corporation and all the participants of the study and the health checkups.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.orcp.2019.03.004.

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