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Effect of pre-pregnancy maternal BMI on adverse pregnancy and neonatal outcomes: results from a multi-ethnic population

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Abstract

Objectives Given the small number of studies on the topic, we aimed to identify the impact of pre-pregnancy maternal body mass index (BMI) on adverse pregnancy outcomes (POs) in a low-risk, multiethnic population, and to calculate related population attributable fractions (PAFs).

Methods This retrospective cohort study included 1134 nulliparous women of 50 nationalities (classified into Arab and non-Arab ethnicity) in Qatar who had their first antenatal visit at a Primary Health Care Corporation (PHCC) facility in June 2016-March 2017 and their PO at a Hamad Medical Corporation (HMC) facility before 10 November 2017. We used multiple imputation to handle missing values and multivariate logistic regression to calculate adjusted odds ratios (aOR) for adverse POs in overweight and obese women.

Results Overweight and obese Arab women were at high risk for gestational diabetes mellitus (GDM) (aOR=2.38, 95%CI 1.51–3.84) and cesarean section (aOR=1.57, 95%CI 1.00–2.48). Obese non-Arab women were at high risk for preeclampsia (aOR=3.83, 95%CI 1.00–15.00). PAFs showed that 41.63% of preeclampsia, 17.36% of pregnancy-induced hypertension, 17.17% of large for gestational age, 15.89% of preterm deliveries, 14.75% of GDM, and 13.99% of cesarean sections could be avoided if all mothers had normal pre-pregnancy BMI. There were no major differences in PAFs by ethnicity.

Conclusion Adverse POs were attributable to maternal obesity. This suggests that, in contrast to existing PHCC protocol, overweight and obese women in Qatar should be targeted earlier in their pregnancy; preferably prior to getting pregnant. We observed ethnic differences in the risk of adverse POs.

Strengths and Limitations of this Study

- Overweight and obese nulliparous mothers who are at risk of maternal and neonatal complications and who attended PHCC between June were identified using body mass index cut offs specific for a multi-ethnic diverse population.
- Risks of maternal and neonatal complications were compared between Arab and Non-Arab maternal ethnic groups
- The method of multiple imputation was used to handle missingness of incomplete variables
- The study used nationality as a surrogate for ethnicity which was valid in this sample given the dichotomous nature of the grouping used.
- Information was not available on socioeconomic status a known potential confounder.

INTRODUCTION

More than half of women of child bearing age in the developed world are either overweight or obese[1], and the percentage of women who are obese at their first antenatal visit nearly doubled between 1990 and 2004[2]. Maternal obesity has been associated with infertility and can cause spontaneous pregnancy loss in early gestation[3]. Gestational diabetes[4], preeclampsia[5], gestational hypertension, depression, instrumental vaginal delivery, cesarean section delivery[6], and surgical site infection have been associated with maternal obesity[7]. Maternal obesity can also impact neonatal outcomes, such as pre-term birth, large for gestational age babies, fetal defects, congenital anomalies, and perinatal death. Length of hospital stay was also reported as an adverse outcome of maternal obesity[7].

Most published studies on the effect of obesity on pregnancy outcomes have focused on primarily homogenous regional populations that are not ethnically diverse[8], but some researchers have shown that ethnic differences can have an impact on the association between obesity and adverse pregnancy outcomes[9]. This impact is particularly relevant for countries like Qatar, which has a diverse, multiethnic, transient population. The 2012 World Health Organization (WHO) STEPwise approach to Surveillance survey for Qatar showed that 68.3% of adult females were overweight and 43.2% were obese[10], highlighting the significance of the maternal obesity problem in the country. The public health care system in Qatar is broken down into primary and secondary/tertiary care systems, with primary care administered by the Primary Health Care Corporation (PHCC), and secondary/tertiary care administered by the Hamad Medical Corporation (HMC). Both systems classify pregnancies as high-risk when the mother is obese Class II or higher (body mass index [BMI] $\geq$40 kg/m^2), has a pre-existing medical condition, and/or obstetric complications, as per the guidelines of the Ministry of Health. Women with high-risk pregnancies

are directly referred to dedicated antenatal clinics of the HMC for specialized management. However, women with a BMI <40 kg/m^2, but who are still overweight or obese, are cared for through the PHCC; they are referred to the HMC only if they develop complications or for delivery.

Population attributable fractions (PAFs) are used to identify the burden of risk factors for a disease or condition in a given population[11]. Few studies have looked at PAFs of maternal obesity [12]. Obesity is highly prevalent in Qatar, hence it is critical to study PAFs associated with obesity in different ethnic groups to quantify the burden of disease that can be attributed to obesity, and thereby help develop targeted management strategies. We aimed to identify the impact of pre-pregnancy maternal BMI on adverse pregnancy outcomes in a low-risk, multiethnic population, and to calculate related PAFs.

METHODS

The PHCC Database is linked to the Birth Register of Qatar; it includes information on all PHCC visits, and thus includes pre-pregnancy and maternal characteristics (e.g., age, nationality, pre-existing conditions), and pregnancy and neonatal outcomes. For this retrospective cohort study, we used the PHCC Database to identify all nulliparous women with singleton pregnancies who had their first antenatal visit at a PHCC facility between 1 June 2016 and 1 March 2017 and their pregnancy outcome at a HMC facility before 10 November 2017 (n=1245). We wanted to target women with low-risk pregnancies as defined by the Ministry of Health of Qatar. Therefore we excluded women with high-risk pregnancies, i.e., those with a pregnancy outcome prior to 24 weeks of gestation (n=8), those who were obese Class II and higher (BMI ≥40 kg/m^2, n=80), or who were under the age of 18 at their first antenatal visit (n=23). Women who gave birth to babies with indeterminate sex (n=2), or who experienced still birth (n=3), fetal death (n=4), or neonatal death (n=1) were also excluded. Among the exclusions were 10 women who met more than one exclusion criterion; therefore, the final study sample consisted of 1,134 women. Ethical approval was obtained from Qatar Primary Health Care Corporation (PHCC) (No: PHCC/RS/17/07/007) and from the Institutional Review Board (IRB) at Qatar University (No:. QU-IRB 846-E/17).

Patient and Public Involvement

This study involved secondary analysis of data collected by PHCC during its routine interactions with the patients. No additional patient or public contact was undertaken in this study.

Maternal ethnicity

Included women were of 50 unique nationalities, and maternal ethnicity was categorized as Arab or non-Arab based on nationality. Women were designated as Arab if they were citizens of one of the 22 countries included in the list of League of Arab States (LAS)[13]. Our Arab study women came from 18 of these countries (Algeria, Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Sudan, Syria, Tunis, United Arab Emirates, and Yemen). The LAS have a common language (Arabic) and share a number of cultural, social, and dietary habits which may put them at different lifestyle and obesity-related risks as compared to non-Arabs. Women of other nationalities were designated as non-Arabs.

Pre-pregnancy body mass index

Pre-pregnancy BMI was calculated based on information recorded at the most recent pre-pregnancy visit available in the PHCC Database, and categorized as normal weight (BMI <25 kg/m^2) overweight (BMI 25-29.99 kg/m^2), and obese (BMI ≥30) based on standard WHO guidelines[14]. However, different BMI cut-offs were applied to Asians (n=405, overweight: BMI 23-27.5 kg/m^2; obese: BMI ≥27.5 kg/m^2), as recommended by the WHO expert consultation[15]. Sensitivity analyses, the results of which are not presented in this manuscript, showed that our application of different BMI cut-offs for Asians was valid, as using standard cut-offs underestimated the risk in that population.

Adverse pregnancy outcomes, adverse neonatal outcomes, and risk factors

Investigated adverse pregnancy outcomes included GDM, pregnancy-induced hypertension (PIH), preeclampsia, preterm delivery, assisted vaginal delivery, and cesarean section. Investigated

adverse neonatal outcomes included macrosomia, large for gestational age, small for gestational age, neonatal intensive care unit referrals, and Apgar score <7 at 1 minute. Risk factors considered included maternal age, maternal ethnicity, and pre-existing conditions such as diabetes mellitus type 1 or 2, hypertension, and thyroid conditions.

Statistical analysis

Maternal characteristics and risk factors were tabulated using the observed data, and differences in the demographics across BMI categories were compared using Pearson's chi squared test. Thereafter, as pre-pregnancy BMI was not available for 101 (8.9%) of the study subjects, multiple imputation was performed to assign these values, with the underlying assumption that BMI values were missing at random[17 18]. Univariate and multivariate associations between maternal BMI category and adverse pregnancy and neonatal outcomes were assessed by logistic regression, using the imputed dataset.

Known and potential risk factors such as maternal age at first antenatal visit, pre-existing diabetes mellitus type 1 or 2, pre-existing hypertension, and pre-existing thyroid conditions were included as covariates in the final model. Maternal ethnicity was assessed as potential risk factor while computing adjusted odds ratios (ORs) for associations between BMI category and adverse pregnancy and neonatal outcomes. Subgroup analysis was conducted by computing crude and adjusted ORs for adverse pregnancy and neonatal pregnancy outcomes separately for Arab and Non-Arab mothers.

The adjusted ORs were used to compute PAFs of overweight and obesity for Arab and non-Arab mothers. PAFs were used to estimate the proportion of adverse pregnancy and neonatal outcomes that could be prevented if either one of two scenarios were true[16]: 1) if overweight and

obese women were all of normal weight before pregnancy; 2) if overweight and obese mothers had a one-category drop in BMI before pregnancy (i.e., obese to overweight, and overweight to normal weight). Scenario 0 was denoted the reference scenario, i.e., the current population as represented by the data. These scenarios were also analysed by ethnicity.

PAFs and corresponding 95% confidence intervals (CIs) were computed using a user-written procedure (punaf) in the Stata software[16]. All analyses in this research report were performed using the Stata 15[19] software package and Microsoft Excel. The significance level for this study was set at 5%, so p-value ≤0.05 was considered statistically significant.

RESULTS

In our study sample, 86.33% of women were aged 18-30 years and 59.17% were of Arab ethnicity. The study sample included women from 50 countries, representing an extremely diverse data set. The most common risk factor among obese women was pre-existing thyroid conditions (5.22%). Term deliveries (gestational age 37-41 weeks) accounted for 89.77% of births in the study sample (Table 1a).

GDM was the most common adverse pregnancy outcome and was observed in 35.89% of the study sample, followed by cesarean section (24.96%). Preeclampsia was observed in 3.44% of the study sample. The prevalence of GDM, cesarean section, and preeclampsia increased with increasing BMI category (Table 1b).

Obese Arab mothers had statistically significant, higher odds of developing GDM (adjusted OR=2.41, 95% CI 1.51–3.84, p <0.01) when compared to normal-weight Arab mothers. Although the odds were higher for obese non-Arab mothers when compared to their normal-weight

counterparts (adjusted OR=1.58, 95% CI 0.96–2.62, p=0.07), these odds were not as high as those observed for Arab mothers, and the association was not statistically significant. Obese non-Arab women showed significantly higher odds (adjusted OR=3.83, 95% CI 0.98–15.00, p=0.05) of developing preeclampsia when compared to normal-weight non-Arab women. Finally, the odds of cesarean section were significant among overweight Arab mothers, as compared to their normal-weight counterparts (adjusted OR=1.57, 95% CI 1.00–2.48, p=0.05), but this association was not significant among obese Arab mothers or among obese non-Arab mothers when compared to their normal-weight counterparts (Table 2). Although higher odds were observed in overweight and obese mothers in both ethnic groups (Figure 1), p-values were not statistically significant for most adverse pregnancy or neonatal outcomes when compared to normal-weight counterparts.

Population attributable fractions

For preeclampsia, a one-category reduction in BMI among Arab mothers corresponded to a PAF of 46.28% for obese women and 38.61% for overweight women. For PIH, a one-category drop in BMI for obese women corresponded to a PAF of 50.83%, meaning that 50.83% of PIH cases could be avoided if obese mothers reduced their BMI category to overweight. Corresponding PAFs for neonatal outcomes were 65.23% for macrosomia and 30.42% for Apgar score <7 at 1 minute. Some of the CIs and PAFs were negative (e.g., small for gestational age and assisted vaginal delivery), indicating a protective effect of obesity on these outcomes, which means that removing obesity could increase these risks (Tables 3 and 4).

For GDM, a one-category reduction in BMI corresponded to a PAF of 24.72% and 24.58% for obese Arab and non-Arab mothers, respectively. The PAF for macrosomia if all women were of normal weight before pregnancy was 13.73% for non-Arab women, and 6.78% for Arab

mothers. The PAFs for neonatal outcomes after a one-category reduction in BMI are not shown in the Figure, as they are mostly negative due to the small number of cases.

DISCUSSION

Our study confirms that there is an association between pre-pregnancy maternal BMI and adverse pregnancy and neonatal pregnancy outcomes in multiethnic populations, using adjusted ORs and PAFs. Previous studies have shown similar strengths of association between overweight and obesity and GDM[20], PIH[20 23], preterm delivery[12 22], assisted vaginal delivery[20 21], cesarean section[20 21], macrosomia[12], large for gestational age[22] and small for gestation age[21 22]. However, the present study found much higher ORs for preeclampsia in non-Arab mothers. This could be attributed to the large portion of Asian mothers in the non-Arab group, who have been reported to be susceptible to preeclampsia[24].

Our results confirm those of a recent study on nulliparous women in Qatar, which reported a higher incidence of GDM, cesarean section, and PIH in obese women[25], whereas overweight women were reported to have higher cesarean section rates only[25]. However, the overall incidence of these outcomes was much lower than in our study sample (GDM: 15% vs 35.89% in our study sample; cesarean section: 16% vs 24.98%). These difference cannot be explained by the data alone, since the earlier study[25] was carried out in a tertiary care setting, whereas this research focused on primary care settings.

The PAFs we report are much higher than those from some published studies[12], due to the high prevalence of overweight and obesity (i.e., exposure) in our study sample. Preeclampsia stands out, as any reduction in BMI category yielded a substantial reduction in the burden of this

condition. A one-category reduction in BMI showed a much higher possibility of disease reduction among obese women than among overweight women, whether they were Arab or non-Arab. However, cesarean section was an exception to this trend, and showed a lesser PAF for a one-category reduction in BMI among obese women than overweight women. This can be explained by the higher OR for cesarean section in overweight women as compared to obese women in both ethnic groups. It should be noted that a causal relationship between exposures and outcomes is generally assumed in PAF calculations. However, this relationship may not necessarily exist, and PAFs should be considered accordingly.

Unlike other reports, the exposure variable in our study was not self-reported. We used standard WHO recommended BMI cut-offs, except in the Asian population, in which Asian-specific cut-offs were applied. Results of a sensitivity analysis indicated that the use of these Asian-specific cut-offs is indeed clinically important in multiethnic populations. Indeed, Asian mothers must be classified as overweight and obese using the WHO-recommended cut-offs for Asians, otherwise high-risk patients may not be properly identified during antenatal care.

Patient nationality was used as a surrogate for ethnicity, but it is common for people to change their citizenship through immigration, which could have limited the strength of the conclusions of this study. However, a detailed analysis of nationalities revealed that the number of patients claiming citizenship to countries that are most likely targets for migrants was minimal (Canadians=0, Australians=0, Americans=3, British=1, French=1). Therefore, the use of nationality as a surrogate for ethnicity is reasonable and valid for this dataset.

Other reports from Qatar showed higher rates of conditions such as diabetes mellitus and cardiovascular diseases, which were not reflected in our study. These low rates may represent an information bias which did not allow us to properly adjust for potential confounders. Data on

socioeconomic status and health center location were not available; hence it is not possible to attribute missing values to these factors or to any other variables for which data was not available.

GDM, preeclampsia, and cesarean section were significantly associated with pre-pregnancy BMI among our overweight and obese mothers, who are not generally considered to have at-risk pregnancies by the health care system in Qatar. High prevalence of GDM in normal-weight mothers (29.21%) indicates that BMI alone cannot explain the problem, which is instead related to population norms and characteristics. High risk of preeclampsia in overweight and obese mothers, especially among non-Arabs, indicates that early screening and management of hypertensive disorders is needed for this group. This implies that clinical screening is indicated for all mothers regardless of their pre-pregnancy BMI or ethnicity, preferably at the start of pregnancy.

The rate of cesarean section was very high in our study sample (25%), especially considering that pregnancies in overweight and obese women are currently considered low-risk by the health care system in Qatar. The odds of cesarean section were uncharacteristically high and similar in overweight and obese mothers regardless of ethnicity. Clinical implications cannot be drawn from these results without properly separating the cesarean sections by their indications (medically necessary vs elective), which were not available in the study sample. Our findings of an association between pre-pregnancy maternal BMI and cesarean section may not properly represent the true nature of the outcome risk and exposure, and should therefore be interpreted with caution.

Adverse pregnancy outcomes were attributable to maternal obesity for even low risk patients. This suggests that, in contrast to the existing PHCC protocol which focuses only on high-risk

pregnancies for intervention, overweight and obese women in Qatar should also be targeted earlier in their pregnancy, preferably prior to getting pregnant. We observed ethnic differences in the risk of adverse pregnancy outcomes. Planning and prevention approaches at the pre-conception stage are needed to raise awareness and reduce the burden of these adverse outcomes on the health care system. There is a need for an ecological approach that addresses societal, cultural, and personal influences by promoting good health at all levels. A top-down approach would work best to formulate public health policy to combat the issues raised. A combination of these public health interventions can help achieve the WHO Non-Communicable Disease Targets for the Global Action Plan by 2025.

Contributors

SS collected data carried out the literature review, and prepared the draft of the paper.
SS and UN planned data analysis and SS implemented statistical analysis.
UN provided input and feedback on the content, data analysis and on the paper draft. SS and UN read and approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Nor required.

Provenance and peer reviewed Not commissioned; externally peer reviewed.

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Figure legends

Figure 1: Adjusted odds ratios and 95% confidence intervals for (a) obese and (b) overweight nulliparous mothers by ethnicity

Figure 2: Population attributable fractions for Arab and non-Arab mothers for pregnancy outcomes for Scenarios 1 (all to normal weight) and Scenario 2 (one-category decrease in body mass index)

Figure 3 : Population attributable fractions for Arab and non-Arab mothers for neonatal outcomes for Scenario 2 (one-category decrease in body mass index)

Tables legends

Table 1(a): Selected characteristics of the study sample by pre-pregnancy maternal body mass index (BMI) in Qatar (N=1134)

Table 1(b): Distribution of adverse pregnancy and neonatal outcomes by pre-pregnancy maternal body mass index (BMI) in Qatar (N=1134)

Table 2: Odds ratios (ORs) and 95% confidence intervals (CIs) of the association between adverse pregnancy and neonatal pregnancy outcomes and body mass index (BMI) category by ethnicity after multiple imputation (N=1134)

Table 3: Population attributable fractions (PAFs) % and 95% confidence intervals (CI) of adverse pregnancy and neonatal outcomes by pre-pregnancy body mass index among Arab mothers

Table 4: Population attributable fractions (PAFs) % and 95% confidence intervals (CI) of adverse pregnancy and neonatal outcomes by pre-pregnancy body mass index among non-Arab mothers

Table 1(a): Selected characteristics of the study sample by pre-pregnancy maternal body mass index (BMI) in Qatar (N=1134)

	Pre-pregnancy BMI category					
	Normal Weight (N=404)	Overweight (N=399)	Obese (N=230)	Missing (N=101)	Total (N=1134)	P-Value
Maternal Age (years)						**<0.001**
18-24	212(52.48%)	141(35.34%)	73(31.74%)	48(47.52%)	474(41.8%)	
25-30	157(38.86%)	195(48.87%)	114(49.57%)	39(38.61%)	505(44.53%)	
31-44	35(8.66%)	63(15.79%)	43(18.7%)	14(13.86%)	155(13.67%)	
Maternal Ethnicity						**0.005**
Arab	254(62.87%)	240(60.15%)	114(49.57%)	63(62.38%)	671(59.17%)	
Non-Arab	150(37.13%)	159(39.85%)	116(50.43%)	38(37.62%)	463(40.83%)	
Pre-existing Hypertension						
Yes	8(1.98%)	10(2.51%)	4(1.74%)	2(1.98%)	24(2.12%)	0.94
No	396(98.02%)	389(97.49%)	226(98.26%)	99(98.02%)	1110(97.88%)	
Pre-existing Diabetes Mellitus Type 1 or 2						
Yes	5(1.24%)	4(1%)	4(1.74%)	0(0%)	13(1.15%)	0.67
No	399(98.76%)	395(99%)	226(98.26%)	101(100%)	1121(98.85%)	
Pre-existing Thyroid Condition						
Yes	18(4.46%)	10(2.51%)	12(5.22%)	2(1.98%)	42(3.7%)	0.22
No	386(95.54%)	389(97.49%)	218(94.78%)	99(98.02%)	1092(96.3%)	
Gestational Age at Delivery (weeks)						
<37	32(7.92%)	40(10.03%)	28(12.17%)	10(9.9%)	110(9.7%)	0.60
37-41	370(91.58%)	357(89.47%)	200(86.96%)	91(90.1%)	1018(89.77%)	
≥42	2(0.5%)	2(0.5%)	2(0.87%)	0(0%)	6(0.53%)	

Values shown as Number(%)

Chi^2 test was used to determine differences across the BMI categories

Fishers Exact test was used when cell count was <5

Table 1(b): Distribution of adverse pregnancy and neonatal outcomes by pre-pregnancy maternal body mass index (BMI) in Qatar (N=1134)

	Pre-pregnancy BMI category					
	Normal Weight (N=404)	**Overweight (N=399)**	**Obese (N=230)**	**Missing (N=101)**	**Total (N=1134)**	**P-Value**
Pregnancy Outcomes						
Gestational Diabetes Mellitus	118(29.21%)	140(35.09%)	108(46.96%)	41(40.59%)	407(35.89%)	**<0.001**
Pregnancy-Induced Hypertension	14(3.47%)	14(3.51%)	17(7.39%)	1(0.99%)	46(4.06%)	**0.038**
Preeclampsia	8(1.98%)	14(3.51%)	15(6.52%)	2(1.98%)	39(3.44%)	**0.013**
Preterm Delivery	32(7.92%)	40(10.03%)	28(12.17%)	8(7.92%)	108(9.52%)	0.21
Assisted Vaginal Delivery	66(16.34%)	62(15.54%)	40(17.39%)	11(10.89%)	179(15.78%)	0.831
Cesarean Section	80(19.8%)	107(26.82%)	69(30%)	27(26.73%)	283(24.96%)	**0.008**
Neonatal Outcomes						
Macrosomia	11(2.72%)	8(2.01%)	13(5.65%)	1(0.99%)	33(2.91%)	**0.034**
Large for Gestational Age	25(6.19%)	31(7.77%)	23(10%)	7(6.93%)	86(7.58%)	0.22
Small for Gestational Age	65(16.09%)	55(13.78%)	32(13.91%)	22(21.78%)	174(15.34%)	0.606
NICU referral	36(8.91%)	46(11.53%)	22(9.57%)	10(9.9%)	114(10.05%)	0.449
Apgar Score <7 at 1 min,	19(4.7%)	17(4.26%)	14(6.09%)	4(3.96%)	54(4.76%)	0.582

Values shown as Number(%)

Chi^2 test was used to determine differences across the BMI categories

Abbreviations: NICU, neonatal intensive care unit.

Table 2: Odds ratios (ORs) and 95% confidence intervals (CIs) of the association between adverse pregnancy and neonatal pregnancy outcomes and body mass index (BMI) category by ethnicity after multiple imputation (N=1134)

	Arabs			Non-Arabs		
	Prevalence	**Adjusted OR (95% CI)**	**P-Value**	**Prevalence**	**Adjusted OR (95% CI)**	**P-Value**
Pregnancy Outcomes						
Gestational Diabetes Mellitus						
Overweight	92(34.98%)	1.24 (0.84 – 1.82)	0.28	64(36.99%)	1.23(0.76 – 2.00)	0.40
Obese	66(51.97%)	2.38 (1.51 – 3.84)	**<0.01**	54(43.2%)	1.60 (0.97 – 2.65)	0.07
Pregnancy-Induced Hypertension						
Overweight	11(4.18%)	1.66 (0.63 – 4.38)	0.31	3(1.73%)	0.41 (0.11 – 1.61)	0.20
Obese	4(3.15%)	1.21 (0.34 – 4.31)	0.76	13(10.4%)	2.41 (0.93 – 6.327)	0.07
Preeclampsia						
Overweight	6(2.28%)	1.11 (0.33 – 3.71)	0.86	9(5.2%)	2.56 (0.66 – 9.97)	0.18
Obese	7(5.51%)	2.64 (0.81 – 8.65)	0.11	8(6.4%)	3.83 (0.98 – 15.00)	**0.05**
Preterm Delivery						
Overweight	26(9.89%)	1.26 (0.66 – 2.41)	0.48	18(10.4%)	1.22 (0.57 – 2.61)	0.61
Obese	14(11.02%)	1.35 (0.63 – 2.91)	0.45	17(13.6%)	1.69 (0.78 – 3.68)	0.18
Assisted Vaginal Delivery						
Overweight	38(14.45%)	0.94 (0.57 – 1.55)	0.82	28(16.18%)	0.87 (0.48 – 1.58)	0.65
Obese	20(15.75%)	1.01 (0.55 – 1.86)	0.97	22(17.6%)	0.97 (0.52 – 1.81)	0.93
Cesarean Section						
Overweight	66(25.1%)	1.57 (1.00 – 2.48)	**0.05**	51(29.48%)	1.05 (0.64 – 1.74)	0.83
Obese	32(25.2%)	1.46 (0.83 – 2.53)	0.20	45(36%)	1.43 (0.84 – 2.44)	0.19
Neonatal Outcomes						
Macrosomia						
Overweight	7(2.66%)	0.86 (0.30 – 2.42)	0.77	1(0.58%)	0.37 (0.04 – 3.39)	0.38
Obese	6(4.72%)	1.48 (0.49 – 4.48)	0.49	7(5.6%)	3.05 (0.77 – 12.06)	0.11
Large for Gestational Age						
Overweight	19(7.22%)	1.06 (0.53 – 2.14)	0.87	15(8.67%)	1.52 (0.61 – 3.79)	0.37
Obese	13(10.24%)	1.46 (0.66 – 3.20)	0.35	12(9.6%)	1.75 (0.70 – 4.41)	0.23
Small for Gestational Age						
Overweight	34(12.93%)	0.84 (0.49 – 1.43)	0.52	30(17.34%)	0.93 (0.52 – 1.67)	0.82
Obese	17(13.39%)	0.90 (0.44 – 1.82)	0.77	19(15.2%)	0.84 (0.44 – 1.60)	0.59
NICU referral						
Overweight	26(9.89%)	1.15 (0.63 – 2.11)	0.65	23(13.29%)	1.30 (0.64 – 2.64)	0.46
Obese	8(6.3%)	0.64 (0.26 – 1.55)	0.32	17(13.6%)	1.30 (0.61 – 2.77)	0.49
Apgar Score <7 at 1 min.						
Overweight	13(4.94%)	1.24 (0.53 – 2.92)	0.63	6(3.47%)	0.59 (0.19 – 1.80)	0.47
Obese	8(6.3%)	1.72 (0.66 – 4.46)	0.27	6(4.8%)	0.86 (0.30 – 2.48)	0.50

For each ethnic group, normal weight was considered the reference category (OR = 1) for calculating ORs.
All outcomes were adjusted for maternal age at first antenatal visit. In addition: pre-eclampsia for pre-existing diabetes, and pre-existing hypertension, preterm delivery for pre-existing comorbid conditions, assisted vaginal delivery for pre-existing comorbid conditions, cesarean section for pre-existing comorbid conditions, macrosomia for pre-existing diabetes, large for gestational age for pre-existing diabetes, and small for gestational age was adjusted for pre-existing diabetes and pre-existing hypertension. NICU, neonatal intensive care unit.

Table 3: Population attributable fractions (PAFs) % and 95% confidence intervals (CI) of adverse pregnancy and neonatal outcomes by pre-pregnancy body mass index among Arab mothers

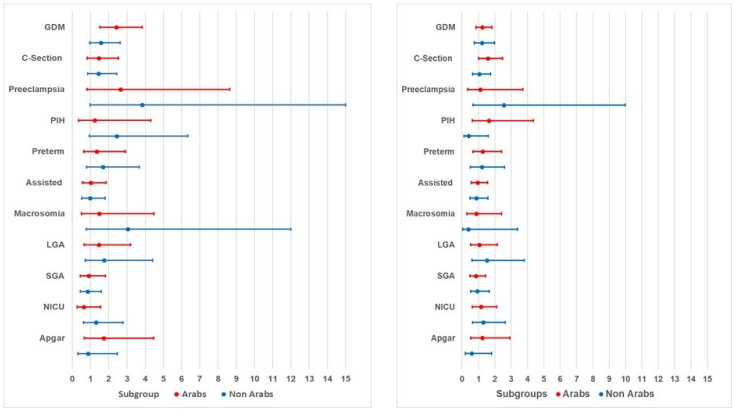
	All to Normal Weight (Scenario 1)	Obese to Overweight (Scenario 2)	Overweight to Normal (Scenario 2)
Pregnancy Outcomes			
Gestational Diabetes	13.64 (2.81 to 23.27)	24.72 (8.88 to 37.8)	12.52 (-7.28 to 28.66)
Pregnancy-Induced Hypertension	14.62 (-28.68 to 43.35)	**50.83 (1.46 to 75.46)**	-3.46 (-116.78 to 50.63)
Preeclampsia	**40.26 (-8.34 to 67.06)**	**46.28 (-8.98 to 73.52)**	**38.61 (-45.72 to 74.14)**
Preterm Delivery	15.04 (-11.09 to 35.03)	16.02 (-33.05 to 46.99)	18.14 (-28.65 to 47.91)
Assisted Vaginal Delivery	-3.11 (-22.13 to 12.95)	8.23 (-32.19 to 36.29)	-8.5 (-50.1 to 21.57)
Cesarean Section	14.09 (-0.9 to 26.86)	7.14 (-21.13 to 28.81)	19.24 (-5.27 to 38.03)
Neonatal Outcomes			
Macrosomia	6.78 (-47.09 to 40.91)	**65.23 (17.74 to 85.31)**	-44.54 (-257.57 to 41.58)
Large for Gestational Age	16.03 (-13.93 to 38.11)	22.26 (-29.92 to 53.48)	17.23 (-38.3 to 50.46)
Small for Gestational Age	-7.96 (-27.51 to 8.59)	-1.19 (-53.4 to 33.24)	-14.47 (-61.48 to 18.85)
NICU referral	7.91 (-18.08 to 28.18)	-25.28 (-104.33 to 23.18)	18.37 (-24.71 to 46.57)
Apgar Score <7 at 1 min.	1.67 (-37.59 to 29.73)	**30.42 (-38.63 to 65.08)**	-10.89 (-111.84 to 41.95)

Abbreviations: NICU, neonatal intensive care unit

Table 4: Population attributable fractions (PAFs) % and 95% confidence intervals (CI) of adverse pregnancy and neonatal outcomes by pre-pregnancy body mass index among non-Arab mothers

	All to Normal Weight	Obese to Overweight	Overweight to Normal
Pregnancy Outcomes			
Gestational Diabetes	16.2 (4.79 to 26.23)	24.58 (8.6 to 37.77)	12.18 (-7.12 to 28)
Pregnancy -Induced Hypertension	19.98 (-26.05 to 49.2)	**50.24 (1.25 to 74.93)**	-3.41 (-114.55 to 50.16)
Preeclampsia	**42.92 (-5.47 to 69.11)**	**46.42 (-9.27 to 73.73)**	**37.79 (-44.56 to 73.23)**
Preterm Delivery	16.89 (-10.67 to 37.59)	15.8 (-32.54 to 46.51)	17.86 (-28.14 to 47.34)
Assisted Delivery	-2.81 (-23.22 to 14.22)	8.14 (-31.83 to 36)	-8.27 (-48.48 to 21.06)
Cesarean Section	13.89 (-0.47 to 26.2)	6.48 (-18.95 to 26.47)	17.19 (-4.73 to 34.53)
Neonatal Outcomes			
Macrosomia	13.73 (-46.3 to 49.13)	**65.86 (17.93 to 85.8)**	-45.01 (-261.54 to 41.84)
Large for Gestational Age	18.86 (-13.59 to 42.04)	22.44 (-30.35 to 53.85)	17.29 (-38.52 to 50.62)
Small for Gestational Age	-8.73 (-30.31 to 9.27)	-1.13 (-50.1 to 31.86)	-13.69 (-57.58 to 17.98)
NICU referral	7.09 (-20.53 to 28.37)	-24.49 (-100.23 to 22.59)	17.79 (-23.81 to 45.41)
Apgar Score < 7	4.25 (-40 to 34.51)	**30.53 (-38.95 to 65.27)**	-10.93 (-112.38 to 42.06)

Abbreviations: NICU, neonatal intensive care unit



Adjusted odds ratios and 95% confidence intervals for (a) obese and (b) overweight nulliparous mothers by ethnicity

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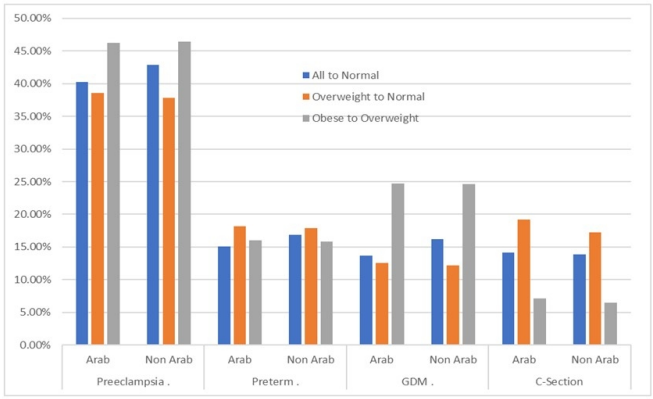
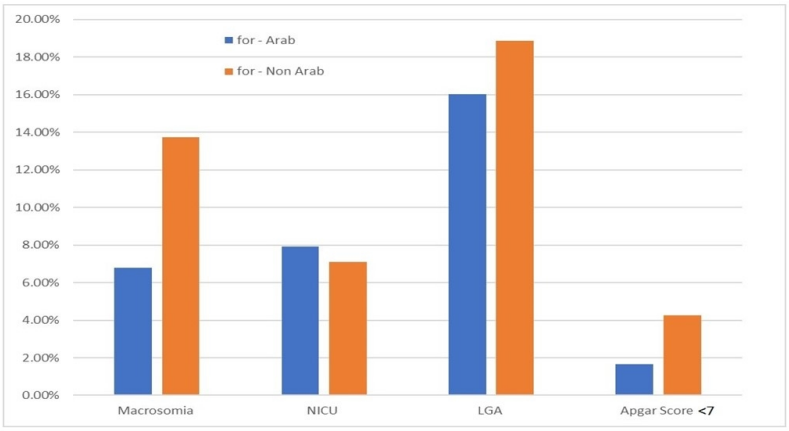


Population attributable fractions for Arab and non-Arab mothers for pregnancy outcomes for Scenarios 1 (all to normal weight) and Scenario 2 (one-category decrease in body mass index)

338x190mm (96 x 96 DPI)



Population attributable fractions for Arab and non-Arab mothers for neonatal outcomes for Scenario 2 (one-category decrease in body mass index)

338x190mm (96 x 96 DPI)

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Effect of Pre-pregnancy maternal BMI on adverse pregnancy and neonatal outcomes: Results from a retrospective cohort study of a multi-ethnic population in Qatar

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Abstract

Background Given the small number of studies on the topic, we aimed to identify the impact of pre-pregnancy maternal body mass index (BMI) on adverse pregnancy outcomes (POs) in a low-risk, multiethnic population, and to calculate related population attributable fractions (PAFs).

Methods This retrospective cohort study included 1134 nulliparous women of 50 nationalities (classified into Arab and non-Arab ethnicity) in Qatar who had their first antenatal visit at a Primary Health Care Corporation (PHCC) facility in June 2016-March 2017 and their PO at a Hamad Medical Corporation (HMC) facility before 10 November 2017. We used multiple imputation to handle missing values and multivariate logistic regression to calculate adjusted odds ratios (aOR) for adverse POs in overweight and obese women.

Results Overweight and obese Arab women were at high risk for gestational diabetes mellitus (GDM) (aOR=2.38, 95%CI 1.51–3.84) and caesarean section (aOR=1.57, 95%CI 1.00–2.48). Obese non-Arab women were at high risk for preeclampsia (aOR=3.83, 95%CI 1.00–15.00). PAFs showed that 41.63% of preeclampsia, 17.36% of pregnancy-induced hypertension, 17.17% of large for gestational age, 15.89% of preterm deliveries, 14.75% of GDM, and 13.99% of caesarean sections could be avoided if all mothers had normal pre-pregnancy BMI. There were no major differences in PAFs by ethnicity.

Conclusion Adverse POs were attributable to maternal obesity. This suggests that, in contrast to existing PHCC protocol, overweight and obese women in Qatar should be targeted earlier in their pregnancy; preferably prior to getting pregnant. We observed ethnic differences in the risk of adverse POs.

Article Summary

Strengths and Limitations of this Study

- The study identifies overweight and obese nulliparous mothers who are at risk for maternal and neonatal complications using specific Body Mass Index cut offs applicable for a multi-ethnic diverse population.
- The study compares the risks across Arab and Non-Arab maternal ethnic groups
- The study uses multiple imputation techniques to handle missing BMI data
- The study used nationality as a surrogate for ethnicity which was valid in this sample given the dichotomous nature of the grouping used.
- The study did not consider potential confounders such as socioeconomic status since such data was not available in the dataset.

Background

More than half of women of child bearing age in the developed world are either overweight or obese[1], and the percentage of women who are obese at their first antenatal visit nearly doubled between 1990 and 2004[2]. Maternal obesity has been associated with infertility and can cause spontaneous pregnancy loss in early gestation[3]. Gestational diabetes[4], preeclampsia[5], gestational hypertension, depression, instrumental vaginal delivery, caesarean section delivery[6], and surgical site infection have been associated with maternal obesity[7]. Maternal obesity can also impact neonatal outcomes, such as pre-term birth, large for gestational age babies, fetal defects, congenital anomalies, and perinatal death. Length of hospital stay was also reported as an adverse outcome of maternal obesity[7].

Most published studies on the effect of obesity on pregnancy outcomes have focused on primarily homogenous regional populations that are not ethnically diverse[8], but some researchers have shown that ethnic differences can have an impact on the association between obesity and adverse pregnancy outcomes[9]. This impact is particularly relevant for countries like Qatar, which has a diverse, multiethnic, transient population. The 2012 World Health Organization (WHO) STEPwise approach to Surveillance survey for Qatar showed that 68.3% of adult females were overweight and 43.2% were obese[10], highlighting the significance of the maternal obesity problem in the country. The public health care system in Qatar is broken down into primary and secondary/tertiary care systems, with primary care administered by the Primary Health Care Corporation (PHCC), and secondary/tertiary care administered by the Hamad Medical Corporation (HMC). Both systems classify pregnancies as high-risk when the mother is obese Class III or higher (body mass index [BMI] $\geq$40 kg/m^2), has a pre-existing medical condition, and/or obstetric complications, as per the guidelines of the Ministry of Health. Women with high-risk pregnancies

are directly referred to dedicated antenatal clinics of the HMC for specialized management. However, women with a BMI <40 kg/m^2, but who are still overweight or obese, are cared for through the PHCC; they are referred to the HMC only if they develop complications or for delivery.

Population attributable fractions (PAFs) are used to identify the burden of risk factors for a disease or condition in a given population[11]. Few studies have looked at PAFs of maternal obesity [12]. Obesity is highly prevalent in Qatar, hence it is critical to study PAFs associated with obesity in different ethnic groups to quantify the burden of disease that can be attributed to obesity, and thereby help develop targeted management strategies. We aimed to identify the impact of pre-pregnancy maternal BMI on adverse pregnancy outcomes in a low-risk, multi-ethnic population, and to calculate related PAFs.

Methods

The PHCC Database is linked to the Birth Register of Qatar; it includes information on all PHCC visits, and thus includes pre-pregnancy and maternal characteristics (e.g., age, nationality, pre-existing conditions), and pregnancy and neonatal outcomes. For this retrospective cohort study, we used the PHCC Database to identify all nulliparous women with singleton pregnancies who had their first antenatal visit at a PHCC facility between 1 June 2016 and 1 March 2017 and their pregnancy outcome at a HMC facility before 10 November 2017 (n=1245). We wanted to target women with low-risk pregnancies as defined by the Ministry of Health of Qatar. Therefore we excluded women with high-risk pregnancies, i.e., those with a pregnancy outcome prior to 24 weeks of gestation (n=8), those who were obese Class II and higher (BMI ≥35 kg/m^2, n=80), or who were under the age of 18 at their first antenatal visit (n=23). Women who gave birth to babies with indeterminate sex (n=2), or who experienced still birth (n=3), fetal death (n=4), or neonatal death (n=1) were also excluded. Among the exclusions were 10 women who met more than one exclusion criterion; therefore, the final study sample consisted of 1,134 women. The anonymized data used in this study was provided after the approval of the study by the research section of the PHCC (reference number PHCC/RS/17/07/007) and the Institutional Review Board (IRB) of Qatar University (Reference **QU-IRB 846-E/17**).

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Patient and Public Involvement

This study involved secondary analysis of data collected by PHCC during its routine interactions with the patients. No additional patient or public contact was undertaken in this study.

Maternal ethnicity

Included women were of 50 unique nationalities, and maternal ethnicity was categorized as Arab or non-Arab based on nationality. Women were designated as Arab if they were citizens of one of the 22 countries included in the list of League of Arab States (LAS)[13]. Our Arab study women came from 18 of these countries (Algeria, Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Sudan, Syria, Tunis, United Arab Emirates, and Yemen). The LAS have a common language (Arabic) and share a number of cultural, social, and dietary habits which may put them at different lifestyle and obesity-related risks as compared to non-Arabs. Women of other nationalities were designated as non-Arabs.

Pre-pregnancy body mass index

Pre-pregnancy BMI was calculated based on information recorded at the most recent pre-pregnancy visit available in the Primary Health Care Center Database. If this primary care visit was prior to 12 weeks from the date of the first antenatal visit, the BMI was treated as missing. Pre-pregnancy BMI was categorized as normal weight (BMI <25 kg/m^2) overweight (BMI 25-29.99 kg/m^2), and obese (BMI ≥30) based on standard WHO guidelines[14]. However, different BMI cut-offs were applied to Asians (n=405, overweight: BMI 23-27.5 kg/m^2; obese: BMI ≥27.5 kg/m^2), as recommended by the WHO expert consultation[15]. Sensitivity analyses, the results of which are not presented in this manuscript, showed that our application of different BMI cut-offs for Asians was valid, as using standard cut-offs underestimated the risk in that population.

Adverse pregnancy outcomes, adverse neonatal outcomes, and risk factors

Investigated adverse pregnancy outcomes included GDM, pregnancy-induced hypertension (PIH), preeclampsia, preterm delivery, assisted vaginal delivery, and caesarean section. Investigated adverse neonatal outcomes included macrosomia, large for gestational age, small for gestational age, neonatal intensive care unit referrals, and Apgar score <7 at 1 minute. Risk factors considered included maternal age, maternal ethnicity, and pre-existing conditions such as diabetes mellitus type 1 or 2, hypertension, and thyroid conditions. Retrospective review of patient medical records including doctors' notes were used to identify pre-existing conditions and most adverse outcomes. Diagnosis of macrosomia, LGA and SGA was based off of the Weight Percentiles Calculator available from the WHO website[16 17].

Statistical analysis

Maternal characteristics and risk factors were tabulated using the observed data, and differences in the demographics across BMI categories were compared using Pearson's chi squared test. Thereafter, as pre-pregnancy BMI was not available for 101 (8.9%) of the study subjects, multiple imputation was performed to assign these values, with the underlying assumption that BMI values were missing at random[18 19]. Univariate and multivariate associations between maternal BMI category and adverse pregnancy and neonatal outcomes were assessed by logistic regression, using the imputed dataset.

Known and potential risk factors such as maternal age at first antenatal visit, pre-existing diabetes mellitus type 1 or 2, pre-existing hypertension, and pre-existing thyroid conditions were included as covariates in the final model. Maternal ethnicity was assessed as potential risk factor while computing adjusted odds ratios (ORs) for associations between BMI category and adverse pregnancy and neonatal outcomes. Subgroup analysis was conducted by computing crude and

adjusted ORs for adverse pregnancy and neonatal pregnancy outcomes separately for Arab and Non-Arab mothers.

The adjusted ORs were used to compute PAFs of overweight and obesity for Arab and non-Arab mothers. PAFs were used to estimate the proportion of adverse pregnancy and neonatal outcomes that could be prevented if either one of two scenarios were true[20]: 1) if overweight and obese women were all of normal weight before pregnancy; 2) if overweight and obese mothers had a one-category drop in BMI before pregnancy (i.e., obese to overweight, and overweight to normal weight). Scenario 0 was denoted the reference scenario, i.e., the current population as represented by the data. These scenarios were also analysed by ethnicity.

PAFs and corresponding 95% confidence intervals (CIs) were computed using a user-written procedure (punaf) in the Stata software[20]. All analyses in this research report were performed using the Stata 15[21] software package and Microsoft Excel. The significance level for this study was set at 5%, so p-value ≤0.05 was considered statistically significant.

Results

In our study sample, 86.33% of women were aged 18-30 years and 59.17% were of Arab ethnicity. The study sample included women from 50 countries, representing an extremely diverse data set. The most common risk factor among obese women was pre-existing thyroid conditions (5.22%). Term deliveries (gestational age 37-41 weeks) accounted for 89.77% of births in the study sample (Table 1a).

==Insert Table 1(a) here ===

GDM was the most common adverse pregnancy outcome and was observed in 35.89% of the study sample, followed by cesarean section (24.96%). Preeclampsia was observed in 3.44% of the study sample. The prevalence of GDM, cesarean section, and preeclampsia increased with increasing BMI category (Table 1b).

== Insert Table 1(b) here ==

Obese Arab mothers had statistically significant, higher odds of developing GDM (adjusted OR=2.41, 95% CI 1.51–3.84, p <0.01) when compared to normal-weight Arab mothers. Although the odds were higher for obese non-Arab mothers when compared to their normal-weight counterparts (adjusted OR=1.58, 95% CI 0.96–2.62, p=0.07), these odds were not as high as those observed for Arab mothers, and the association was not statistically significant. Obese non-Arab women showed significantly higher odds (adjusted OR=3.83, 95% CI 0.98–15.00, p=0.05) of developing preeclampsia when compared to normal-weight non-Arab women. Finally, the odds of caesarean section were significant among overweight Arab mothers, as compared to their normal-weight counterparts (adjusted OR=1.57, 95% CI 1.00–2.48, p=0.05), but this association was not significant among obese Arab mothers or among obese non-Arab mothers when compared to their normal-weight counterparts (Table 2). Although higher odds were observed in obese (Figure 1)and overweight (Figure 2) mothers in both ethnic groups, p-values were not statistically significant for most adverse pregnancy or neonatal outcomes when compared to normal-weight counterparts.

==Insert Table 2 here===

== Insert Figure 1 here==

== Insert Figure 2 here==

Population attributable fractions

For preeclampsia, a one-category reduction in BMI among Arab mothers corresponded to a PAF of 46.28% for obese women and 38.61% for overweight women (Figure 3). For PIH, a one-category drop in BMI for obese women corresponded to a PAF of 50.83%, meaning that 50.83% of PIH cases could be avoided if obese mothers reduced their BMI category to overweight (Figure 3). Corresponding PAFs for neonatal outcomes were 65.23% for macrosomia and 30.42% for Apgar score <7 at 1 minute. Some of the CIs and PAFs were negative (e.g., small for gestational age and assisted vaginal delivery), indicating a protective effect of obesity on these outcomes, which means that removing obesity could increase these risks (Tables 3 and 4).

== Insert tables 3 and 4 here ==

For GDM, a one-category reduction in BMI corresponded to a PAF of 24.72% and 24.58% for obese Arab and non-Arab mothers, respectively (Figure 3). The PAF for macrosomia if all women were of normal weight before pregnancy was 13.73% for non-Arab women, and 6.78% for Arab mothers (Figure 4). The PAFs for neonatal outcomes after a one-category reduction in BMI are not shown in the Figure 3 and Figure 4, as they are mostly negative due to the small number of cases.

=== Insert Figures 3 and 4 here ==

Discussion

Our study confirms that there is an association between pre-pregnancy maternal BMI and adverse pregnancy and neonatal pregnancy outcomes in multi-ethnic populations, using adjusted ORs and

PAFs. Previous studies have shown similar strengths of association between overweight and obesity and GDM[22], PIH[22 23], preterm delivery[12 24], assisted vaginal delivery[22 25], caesarean section[22 25], macrosomia[12], large for gestational age[24] and small for gestation age[24 25]. However, the present study found much higher ORs for preeclampsia in non-Arab mothers. This could be attributed to the large portion of Asian mothers in the non-Arab group, who have been reported to be susceptible to preeclampsia[26].

Our results confirm those of a recent study on nulliparous women in Qatar, which reported a higher incidence of GDM, caesarean section, and PIH in obese women[27], whereas overweight women were reported to have higher caesarean section rates only[27]. However, the overall incidence of these outcomes was much lower than in our study sample (GDM: 15% vs 35.89% in our study sample; caesarean section: 16% vs 24.98%). These difference cannot be explained by the data alone, since the earlier study[27] was carried out in a tertiary care setting, whereas this research focused on primary care settings.

The PAFs we report are much higher than those from some published studies[12], due to the high prevalence of overweight and obesity (i.e., exposure) in our study sample. Preeclampsia stands out, as any reduction in BMI category yielded a substantial reduction in the burden of this condition. A one-category reduction in BMI showed a much higher possibility of disease reduction among obese women than among overweight women, whether they were Arab or non-Arab. However, caesarean section was an exception to this trend, and showed a lesser PAF for a one-category reduction in BMI among obese women than overweight women. This can be explained by the higher OR for caesarean section in overweight women as compared to obese women in both ethnic groups. It should be noted that a causal relationship between exposures and outcomes is

generally assumed in PAF calculations. However, this relationship may not necessarily exist, and PAFs should be considered accordingly.

Unlike other reports, the exposure variable in our study was not self-reported. We used standard WHO recommended BMI cut-offs, except in the Asian population, in which Asian-specific cut-offs were applied. Results of a sensitivity analysis indicated that the use of these Asian-specific cut-offs is indeed clinically important in multiethnic populations. Indeed, Asian mothers must be classified as overweight and obese using the WHO-recommended cut-offs for Asians, otherwise high-risk patients may not be properly identified during antenatal care.

Patient nationality was used as a surrogate for ethnicity, but it is common for people to change their citizenship through immigration, which could have limited the strength of the conclusions of this study. However, a detailed analysis of nationalities revealed that the number of patients claiming citizenship to countries that are most likely targets for migrants was minimal (Canadians=0, Australians=0, Americans=3, British=1, French=1). Therefore, the use of nationality as a surrogate for ethnicity is reasonable and valid for this dataset.

Other reports from Qatar showed higher rates of conditions such as diabetes mellitus and cardiovascular diseases, which were not reflected in our study. These low rates may represent an information bias which did not allow us to properly adjust for potential confounders. Data on socioeconomic status and health center location were not available; hence it is not possible to attribute missing values to these factors or to any other variables for which data was not available.

GDM, preeclampsia, and cesarean section were significantly associated with pre-pregnancy BMI among our overweight and obese mothers, who are not generally considered to have at-risk pregnancies by the health care system in Qatar. High prevalence of GDM in normal-weight

mothers (29.21%) indicates that BMI alone cannot explain the problem, which is instead related to population norms and characteristics. High risk of preeclampsia in overweight and obese mothers, especially among non-Arabs, indicates that early screening and management of hypertensive disorders is needed for this group. This implies that clinical screening is indicated for all mothers regardless of their pre-pregnancy BMI or ethnicity, preferably at the start of pregnancy.

The rate of cesarean section was very high in our study sample (25%), especially considering that pregnancies in overweight and obese women are currently considered low-risk by the health care system in Qatar. The odds of cesarean section were uncharacteristically high and similar in overweight and obese mothers regardless of ethnicity. Clinical implications cannot be drawn from these results without properly separating the cesarean sections by their indications (medically necessary vs elective), which were not available in the study sample. Our findings of an association between pre-pregnancy maternal BMI and cesarean section may not properly represent the true nature of the outcome risk and exposure, and should therefore be interpreted with caution.

As has been mentioned in above paragraphs, the retrospective cohort nature of this study limited our ability to validate or verify the elements of the dataset and other potential confounders through additional patient contact. The anonymity of the data by design made it impossible to undertake such a follow up. The strength of our findings is therefore directly related to the strength of the dataset used. The number of missing values in the exposure variable, the pre-pregnancy BMI, meant that we were unable to ascertain a direct relationship for those records. However, the impact of such was minimized by using the multiple imputation techniques. The PAFs were computed using the punaf user written extension for Stata software

and manual calculations for such cannot be undertaken due to the computational complexity of the task.

Adverse pregnancy outcomes were attributable to maternal obesity for even low risk patients. This suggests that, in contrast to the existing PHCC protocol which focuses only on high-risk pregnancies for intervention, overweight and obese women in Qatar should also be targeted earlier in their pregnancy, preferably prior to getting pregnant. We observed ethnic differences in the risk of adverse pregnancy outcomes. Planning and prevention approaches at the pre-conception stage are needed to raise awareness and reduce the burden of these adverse outcomes on the health care system. There is a need for an ecological approach that addresses societal, cultural, and personal influences by promoting good health at all levels. A top-down approach would work best to formulate public health policy to combat the issues raised. A combination of these public health interventions can help achieve the WHO Non-Communicable Disease Targets for the Global Action Plan by 2025.

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Contributors Conceptualization, S.S. and U.N.; methodology, S.S. and U.N.; software, S.S.; validation, S.S. and U.N.; formal analysis, S.S.; investigation, S.S. and U.N; resources, S.S.; data curation, S.S.; writing—original draft preparation, S.S.; writing—review and editing, S.S. and U.N.; visualization, S.S. and U.N.; supervision, U.N. ; project administration, S.S.; funding acquisition, U.N.

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Disclaimer All authors have seen and approved the final version of the manuscript being submitted. They warrant that the article is the authors' original work, has not received prior publication and is not under consideration for publication elsewhere.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained from The Primary Health Care Corporation (Reference Number **PHCC/RS/17/07/007)** on October 3, 2017 and the Institutional Review Board (IRB) of Qatar University (Reference **QU-IRB 846-E/17**) on November 11, 2017.

Data availability statement The database analysed for this research include information on all antenatal visits to Primary Health Care Centres, between 1 June 2016 and 1 March 2017. Data can be obtained by request from the Primary Health Corporation in Qatar.

Provenance and peer review Not commissioned; externally peer reviewed.

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Table 1(a): Selected characteristics of the study sample by pre-pregnancy maternal body mass index (BMI) in Qatar (N=1134)

	Pre-pregnancy BMI category					
	Normal Weight (N=404)	Overweight (N=399)	Obese (N=230)	Missing (N=101)	Total (N=1134)	P-Value
Maternal Age (years)						**<0.001**
18-24	212(52.48%)	141(35.34%)	73(31.74%)	48(47.52%)	474(41.8%)	
25-30	157(38.86%)	195(48.87%)	114(49.57%)	39(38.61%)	505(44.53%)	
31-44	35(8.66%)	63(15.79%)	43(18.7%)	14(13.86%)	155(13.67%)	
Maternal Ethnicity						**0.005**
Arab	254(62.87%)	240(60.15%)	114(49.57%)	63(62.38%)	671(59.17%)	
Non-Arab	150(37.13%)	159(39.85%)	116(50.43%)	38(37.62%)	463(40.83%)	
Pre-existing Hypertension						
Yes	8(1.98%)	10(2.51%)	4(1.74%)	2(1.98%)	24(2.12%)	0.94
No	396(98.02%)	389(97.49%)	226(98.26%)	99(98.02%)	1110(97.88%)	
Pre-existing Diabetes Mellitus Type 1 or 2						
Yes	5(1.24%)	4(1%)	4(1.74%)	0(0%)	13(1.15%)	0.67
No	399(98.76%)	395(99%)	226(98.26%)	101(100%)	1121(98.85%)	
Pre-existing Thyroid Condition						
Yes	18(4.46%)	10(2.51%)	12(5.22%)	2(1.98%)	42(3.7%)	0.22
No	386(95.54%)	389(97.49%)	218(94.78%)	99(98.02%)	1092(96.3%)	
Gestational Age at Delivery (weeks)						
<37	32(7.92%)	40(10.03%)	28(12.17%)	10(9.9%)	110(9.7%)	0.60
37-41+6d	370(91.58%)	357(89.47%)	200(86.96%)	91(90.1%)	1018(89.77%)	
≥42	2(0.5%)	2(0.5%)	2(0.87%)	0(0%)	6(0.53%)	

Values shown as Number(%)
Chi^2 test was used to determine differences across the BMI categories
Fishers Exact test was used when cell count was <5

Table 1(b): Distribution of adverse pregnancy and neonatal outcomes by pre-pregnancy maternal body mass index (BMI) in Qatar (N=1134)

	Pre-pregnancy BMI category					
	Normal Weight (N=404)	**Overweight (N=399)**	**Obese (N=230)**	**Missing (N=101)**	**Total (N=1134)**	**P-Value**
Pregnancy Outcomes						
Gestational Diabetes Mellitus	118(29.21%)	140(35.09%)	108(46.96%)	41(40.59%)	407(35.89%)	**<0.001**
Pregnancy-Induced Hypertension	14(3.47%)	14(3.51%)	17(7.39%)	1(0.99%)	46(4.06%)	**0.038**
Preeclampsia	8(1.98%)	14(3.51%)	15(6.52%)	2(1.98%)	39(3.44%)	**0.013**
Preterm Delivery	32(7.92%)	40(10.03%)	28(12.17%)	8(7.92%)	108(9.52%)	0.21
Assisted Vaginal Delivery	66(16.34%)	62(15.54%)	40(17.39%)	11(10.89%)	179(15.78%)	0.831
Cesarean Section	80(19.8%)	107(26.82%)	69(30%)	27(26.73%)	283(24.96%)	**0.008**
Neonatal Outcomes						
Macrosomia	11(2.72%)	8(2.01%)	13(5.65%)	1(0.99%)	33(2.91%)	**0.034**
Large for Gestational Age	25(6.19%)	31(7.77%)	23(10%)	7(6.93%)	86(7.58%)	0.22
Small for Gestational Age	65(16.09%)	55(13.78%)	32(13.91%)	22(21.78%)	174(15.34%)	0.606
NICU referral	36(8.91%)	46(11.53%)	22(9.57%)	10(9.9%)	114(10.05%)	0.449
Apgar Score <7 at 1 min,	19(4.7%)	17(4.26%)	14(6.09%)	4(3.96%)	54(4.76%)	0.582

Values shown as Number(%)

Chi^2 test was used to determine differences across the BMI categories

Abbreviations: NICU, neonatal intensive care unit.

Table 2: Odds ratios (ORs) and 95% confidence intervals (CIs) of the association between adverse pregnancy and neonatal pregnancy outcomes and body mass index (BMI) category by ethnicity after multiple imputation (N=1134)

	Arabs			Non-Arabs		
	Prevalence	Adjusted OR (95% CI)	P-Value	Prevalence	Adjusted OR (95% CI)	P-Value
Pregnancy Outcomes						
Gestational Diabetes Mellitus						
Overweight	92(34.98%)	1.24 (0.84 – 1.82)	0.28	64(36.99%)	1.23(0.76 – 2.00)	0.40
Obese	66(51.97%)	2.38 (1.51 – 3.84)	**<0.01**	54(43.2%)	1.60 (0.97 – 2.65)	0.07
Pregnancy-Induced Hypertension						
Overweight	11(4.18%)	1.66 (0.63 – 4.38)	0.31	3(1.73%)	0.41 (0.11 – 1.61)	0.20
Obese	4(3.15%)	1.21 (0.34 – 4.31)	0.76	13(10.4%)	2.41 (0.93 – 6.327)	0.07
Preeclampsia						
Overweight	6(2.28%)	1.11 (0.33 – 3.71)	0.86	9(5.2%)	2.56 (0.66 – 9.97)	0.18
Obese	7(5.51%)	2.64 (0.81 – 8.65)	0.11	8(6.4%)	3.83 (0.98 – 15.00)	**0.05**
Preterm Delivery						
Overweight	26(9.89%)	1.26 (0.66 – 2.41)	0.48	18(10.4%)	1.22 (0.57 – 2.61)	0.61
Obese	14(11.02%)	1.35 (0.63 – 2.91)	0.45	17(13.6%)	1.69 (0.78 – 3.68)	0.18
Assisted Vaginal Delivery						
Overweight	38(14.45%)	0.94 (0.57 – 1.55)	0.82	28(16.18%)	0.87 (0.48 – 1.58)	0.65
Obese	20(15.75%)	1.01 (0.55 – 1.86)	0.97	22(17.6%)	0.97 (0.52 – 1.81)	0.93
Cesarean Section						
Overweight	66(25.1%)	1.57 (1.00 – 2.48)	**0.05**	51(29.48%)	1.05 (0.64 – 1.74)	0.83
Obese	32(25.2%)	1.46 (0.83 – 2.53)	0.20	45(36%)	1.43 (0.84 – 2.44)	0.19
Neonatal Outcomes						
Macrosomia						
Overweight	7(2.66%)	0.86 (0.30 – 2.42)	0.77	1(0.58%)	0.37 (0.04 – 3.39)	0.38
Obese	6(4.72%)	1.48 (0.49 – 4.48)	0.49	7(5.6%)	3.05 (0.77 – 12.06)	0.11
Large for Gestational Age						
Overweight	19(7.22%)	1.06 (0.53 – 2.14)	0.87	15(8.67%)	1.52 (0.61 – 3.79)	0.37
Obese	13(10.24%)	1.46 (0.66 – 3.20)	0.35	12(9.6%)	1.75 (0.70 – 4.41)	0.23
Small for Gestational Age						
Overweight	34(12.93%)	0.84 (0.49 – 1.43)	0.52	30(17.34%)	0.93 (0.52 – 1.67)	0.82
Obese	17(13.39%)	0.90 (0.44 – 1.82)	0.77	19(15.2%)	0.84 (0.44 – 1.60)	0.59
NICU referral						
Overweight	26(9.89%)	1.15 (0.63 – 2.11)	0.65	23(13.29%)	1.30 (0.64 – 2.64)	0.46
Obese	8(6.3%)	0.64 (0.26 – 1.55)	0.32	17(13.6%)	1.30 (0.61 – 2.77)	0.49
Apgar Score <7 at 1 min.						
Overweight	13(4.94%)	1.24 (0.53 – 2.92)	0.63	6(3.47%)	0.59 (0.19 – 1.80)	0.47
Obese	8(6.3%)	1.72 (0.66 – 4.46)	0.27	6(4.8%)	0.86 (0.30 – 2.48)	0.50

For each ethnic group, normal weight was considered the reference category (OR = 1) for calculating ORs.
All outcomes were adjusted for maternal age at first antenatal visit. In addition: pre-eclampsia for pre-existing diabetes, and pre-existing hypertension, preterm delivery for pre-existing comorbid conditions, assisted vaginal delivery for pre-existing comorbid conditions, caesarean section for pre-existing comorbid conditions, macrosomia for pre-existing diabetes, large for gestational age for pre-existing diabetes, and small for gestational age was adjusted for pre-existing diabetes and pre-existing hypertension.
NICU, neonatal intensive care unit.

Table 3: Population attributable fractions (PAFs) % and 95% confidence intervals (CI) of adverse pregnancy and neonatal outcomes by pre-pregnancy body mass index among Arab mothers

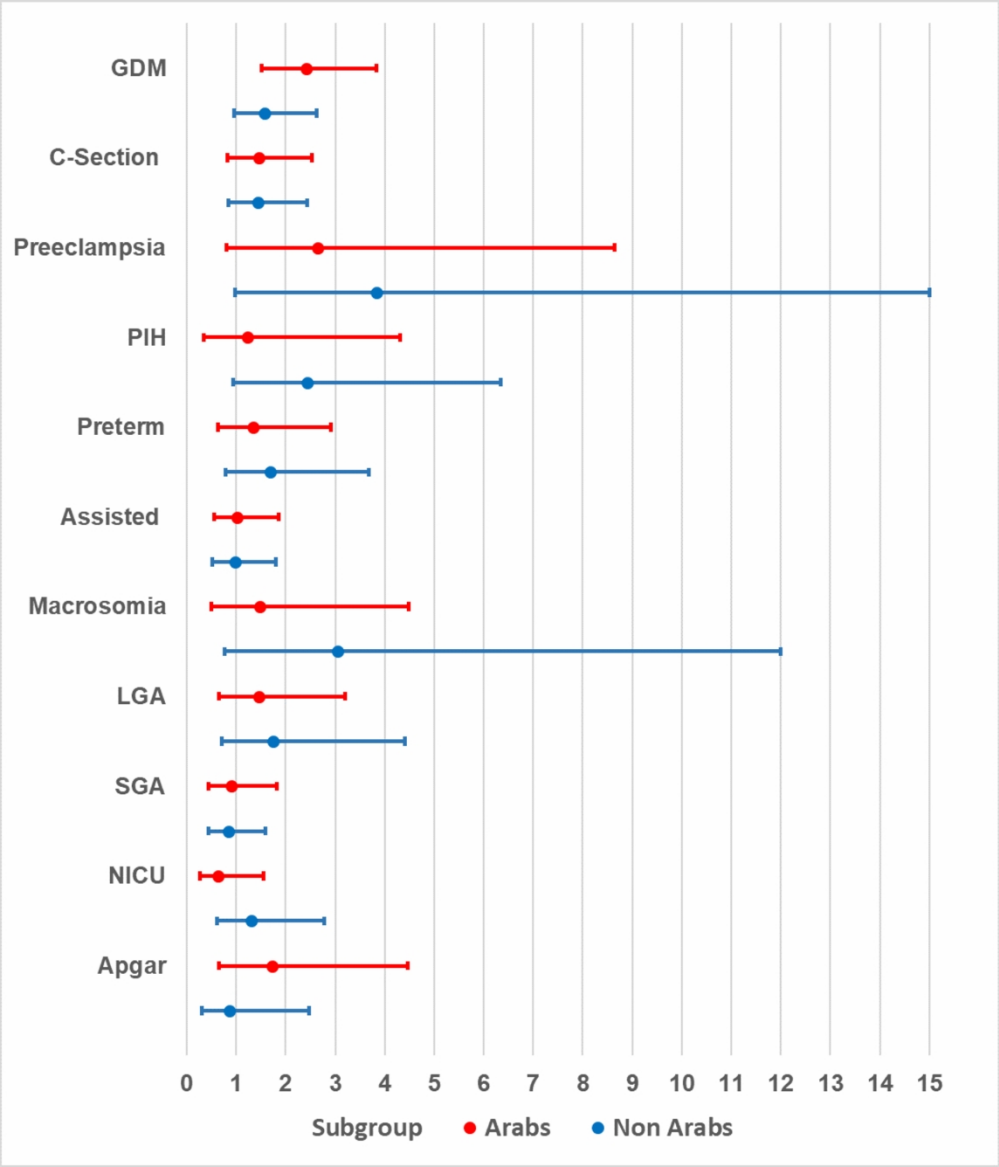
	All to Normal Weight (Scenario 1)	Obese to Overweight (Scenario 2)	Overweight to Normal (Scenario 2)
Pregnancy Outcomes			
Gestational Diabetes	13.64 (2.81 to 23.27)	24.72 (8.88 to 37.8)	12.52 (-7.28 to 28.66)
Pregnancy-Induced Hypertension	14.62 (-28.68 to 43.35)	**50.83 (1.46 to 75.46)**	-3.46 (-116.78 to 50.63)
Preeclampsia	**40.26 (-8.34 to 67.06)**	**46.28 (-8.98 to 73.52)**	**38.61 (-45.72 to 74.14)**
Preterm Delivery	15.04 (-11.09 to 35.03)	16.02 (-33.05 to 46.99)	18.14 (-28.65 to 47.91)
Assisted Vaginal Delivery	-3.11 (-22.13 to 12.95)	8.23 (-32.19 to 36.29)	-8.5 (-50.1 to 21.57)
Cesarean Section	14.09 (-0.9 to 26.86)	7.14 (-21.13 to 28.81)	19.24 (-5.27 to 38.03)
Neonatal Outcomes			
Macrosomia	6.78 (-47.09 to 40.91)	**65.23 (17.74 to 85.31)**	-44.54 (-257.57 to 41.58)
Large for Gestational Age	16.03 (-13.93 to 38.11)	22.26 (-29.92 to 53.48)	17.23 (-38.3 to 50.46)
Small for Gestational Age	-7.96 (-27.51 to 8.59)	-1.19 (-53.4 to 33.24)	-14.47 (-61.48 to 18.85)
NICU referral	7.91 (-18.08 to 28.18)	-25.28 (-104.33 to 23.18)	18.37 (-24.71 to 46.57)
Apgar Score <7 at 1 min.	1.67 (-37.59 to 29.73)	**30.42 (-38.63 to 65.08)**	-10.89 (-111.84 to 41.95)

Abbreviations: NICU, neonatal intensive care unit

Table 4: Population attributable fractions (PAFs) % and 95% confidence intervals (CI) of adverse pregnancy and neonatal outcomes by pre-pregnancy body mass index among non-Arab mothers

	All to Normal Weight	Obese to Overweight	Overweight to Normal
Pregnancy Outcomes			
Gestational Diabetes	16.2 (4.79 to 26.23)	24.58 (8.6 to 37.77)	12.18 (-7.12 to 28)
Pregnancy -Induced Hypertension	19.98 (-26.05 to 49.2)	**50.24 (1.25 to 74.93)**	-3.41 (-114.55 to 50.16)
Preeclampsia	**42.92 (-5.47 to 69.11)**	**46.42 (-9.27 to 73.73)**	**37.79 (-44.56 to 73.23)**
Preterm Delivery	16.89 (-10.67 to 37.59)	15.8 (-32.54 to 46.51)	17.86 (-28.14 to 47.34)
Assisted Delivery	-2.81 (-23.22 to 14.22)	8.14 (-31.83 to 36)	-8.27 (-48.48 to 21.06)
Cesarean Section	13.89 (-0.47 to 26.2)	6.48 (-18.95 to 26.47)	17.19 (-4.73 to 34.53)
Neonatal Outcomes			
Macrosomia	13.73 (-46.3 to 49.13)	**65.86 (17.93 to 85.8)**	-45.01 (-261.54 to 41.84)
Large for Gestational Age	18.86 (-13.59 to 42.04)	22.44 (-30.35 to 53.85)	17.29 (-38.52 to 50.62)
Small for Gestational Age	-8.73 (-30.31 to 9.27)	-1.13 (-50.1 to 31.86)	-13.69 (-57.58 to 17.98)
NICU referral	7.09 (-20.53 to 28.37)	-24.49 (-100.23 to 22.59)	17.79 (-23.81 to 45.41)
Apgar Score < 7	4.25 (-40 to 34.51)	**30.53 (-38.95 to 65.27)**	-10.93 (-112.38 to 42.06)

Abbreviations: NICU, neonatal intensive care unit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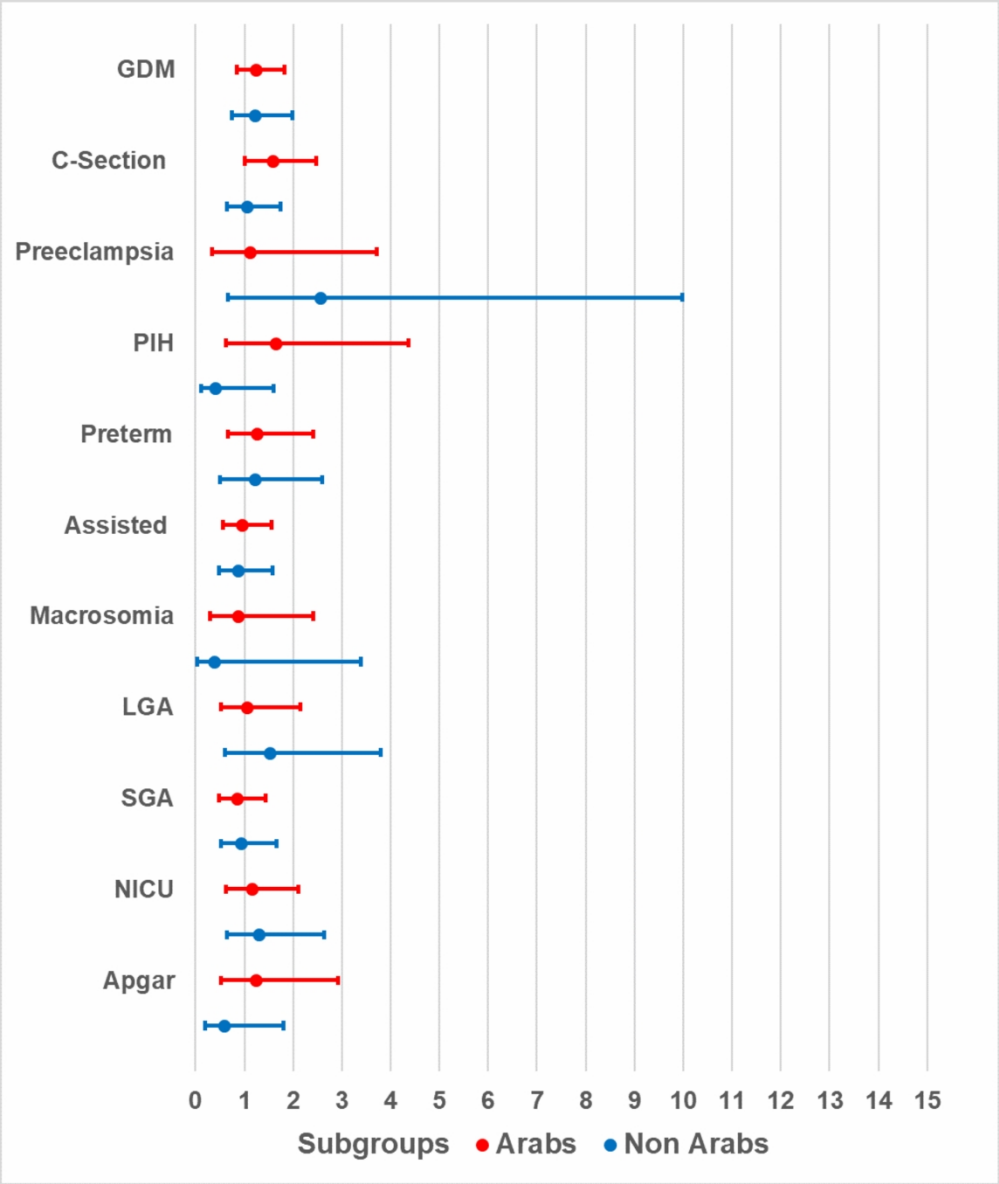
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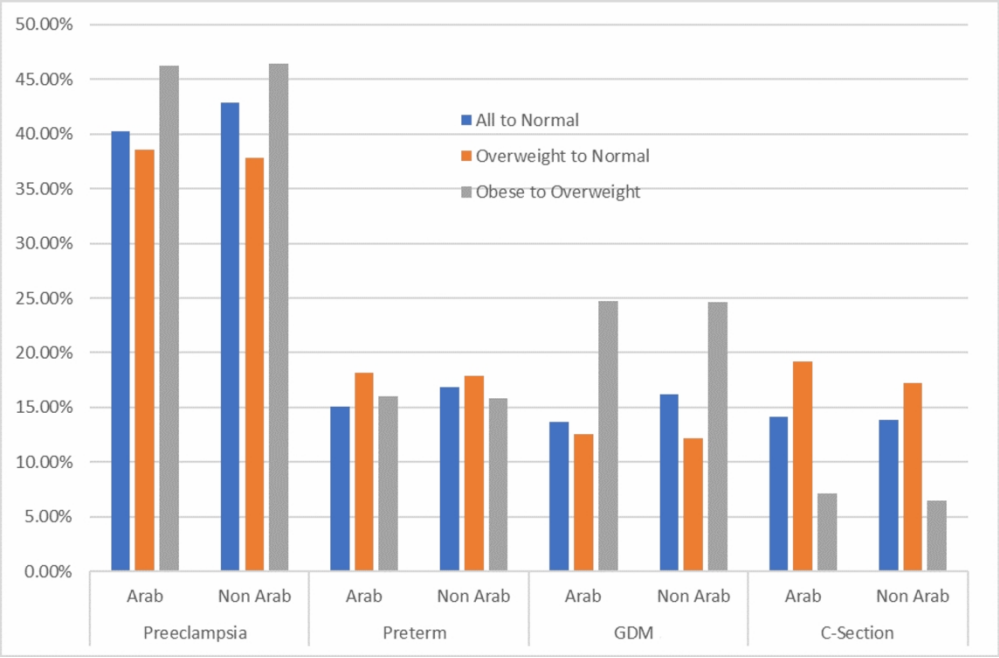
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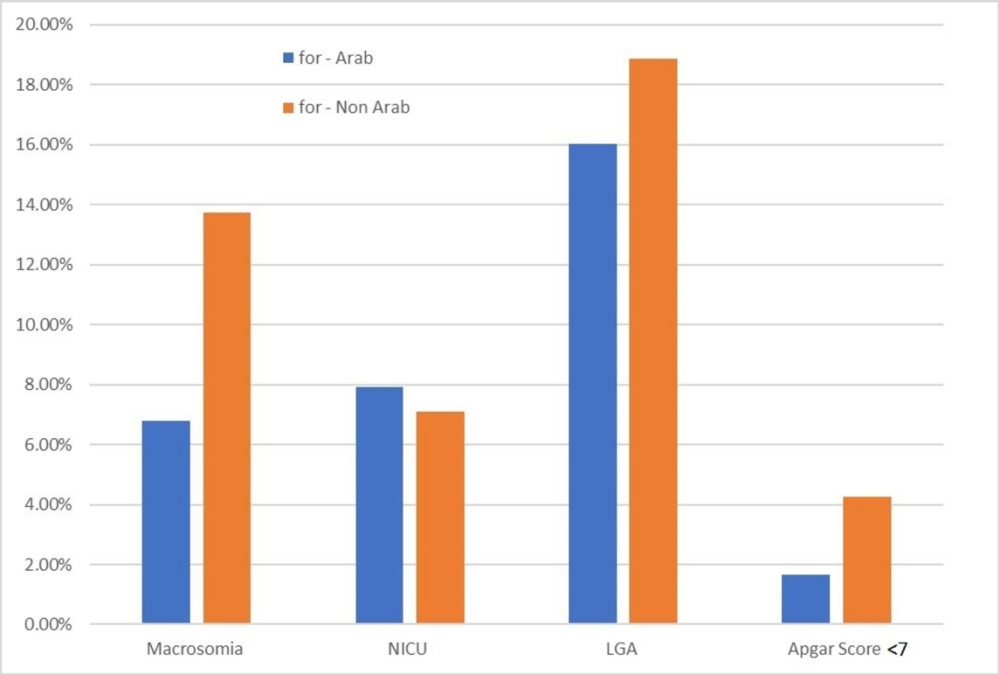
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for - Arab
for - Non Arab
Macrosomia
NICU
LGA
Apgar Score <7

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Done, title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Done, page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Done, page 4
Objectives	3	State specific objectives, including any pre-specified hypotheses Done, page 4
Methods		
Study design	4	Present key elements of study design early in the paper Done, Abstract and page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Done, methods section, page 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Done, methods section, page 6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Done, methods section, page 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Data source and methods of assessment of exposure and outcomes are presented in in the methods section page 6
Bias	9	Describe any efforts to address potential sources of bias Potential sources of bias are explained on page 13
Study size	10	Explain how the study size was arrived at All nulliparous women with singleton pregnancies who had their first antenatal visit at a PHCC facility between 1 June 2016 and 1 March 2017 and their pregnancy outcome at a HMC facility before 10 November 2017 (n=1245) were included in this study, methods section page 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why All quantitative variables included in analysis with details of varaibles that have been categorized are presented in methods section page 6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding Done, all statistical methods to control for confounding on page 8-9
		(*b*) Describe any methods used to examine subgroups and interactions Done, multivariable logistic regression analysis and population attributable fractions were used to adjust for overweight and obesity for Arab and non-Arab mothers , pages 7-8

		(*c*) Explain how missing data were addressed Done, multiple imputation was used to handle missing data, page 8
		(*d*) If applicable, explain how loss to follow-up was addressed Not applicable
		(*e*) Describe any sensitivity analyses Sensitivity analysis was not applied
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Done, methods section page 5
		(b) Give reasons for non-participation at each stage Done, page 5
		(c) Consider use of a flow diagram Flow diagram was not needed
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Done, table 1 and results section page 9-10
		(b) Indicate number of participants with missing data for each variable of interest Done, table 1, results page 9
		(c) Summarise follow-up time (eg, average and total amount) Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures over time Not applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Done, tables 2,3, 4, and results section, pages 10-11
		(*b*) Report category boundaries when continuous variables were categorized Done, page 7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Done, pages 9-10
Discussion		
Key results	18	Summarise key results with reference to study objectives Done, 12-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Done, page 13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Done, pages 14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results Done, page 15
Other information		

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Done, funding statement is presented after discussion

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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Effect of Pre-pregnancy maternal BMI on adverse pregnancy and neonatal outcomes: Results from a retrospective cohort study of a multi-ethnic population in Qatar

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Abstract

Background Given the small number of studies on the topic, we aimed to identify the impact of pre-pregnancy maternal body mass index (BMI) on adverse pregnancy outcomes (POs) in a low-risk, multiethnic population, and to calculate related population attributable fractions (PAFs).

Methods This retrospective cohort study included 1134 nulliparous women of 50 nationalities (classified into Arab and non-Arab ethnicity) in Qatar who had their first antenatal visit at a Primary Health Care Corporation (PHCC) facility in June 2016-March 2017 and their PO at a Hamad Medical Corporation (HMC) facility before 10 November 2017. We used multiple imputation to handle missing values and multivariate logistic regression to calculate adjusted odds ratios (aOR) for adverse POs in overweight and obese women.

Results Overweight and obese Arab women were at high risk for gestational diabetes mellitus (GDM) (aOR=2.38, 95%CI 1.51–3.84) and caesarean section (aOR=1.57, 95%CI 1.00–2.48). Obese non-Arab women were at high risk for preeclampsia (aOR=3.83, 95%CI 1.00–15.00). PAFs showed that 41.63% of preeclampsia, 17.36% of pregnancy-induced hypertension, 17.17% of large for gestational age, 15.89% of preterm deliveries, 14.75% of GDM, and 13.99% of caesarean sections could be avoided if all mothers had normal pre-pregnancy BMI. There were no major differences in PAFs by ethnicity.

Conclusion Adverse POs were attributable to maternal obesity. This suggests that, in contrast to existing PHCC protocol, overweight and obese women in Qatar should be targeted earlier in their pregnancy; preferably prior to getting pregnant. We observed ethnic differences in the risk of adverse POs.

Article Summary

Strengths and Limitations of this Study

- The study identifies overweight and obese nulliparous mothers who are at risk for maternal and neonatal complications using specific Body Mass Index cut offs applicable for a multi-ethnic diverse population.
- The study compares the risks across Arab and Non-Arab maternal ethnic groups
- The study uses multiple imputation techniques to handle missing BMI data
- The study used nationality as a surrogate for ethnicity which was valid in this sample given the dichotomous nature of the grouping used.
- The study did not consider potential confounders such as socioeconomic status since such data was not available in the dataset.

Background

More than half of women of child bearing age in the developed world are either overweight or obese[1], and the percentage of women who are obese at their first antenatal visit nearly doubled between 1990 and 2004[2]. Maternal obesity has been associated with infertility and can cause spontaneous pregnancy loss in early gestation[3]. Gestational diabetes[4], preeclampsia[5], gestational hypertension, depression, instrumental vaginal delivery, caesarean section delivery[6], and surgical site infection have been associated with maternal obesity[7]. Maternal obesity can also impact neonatal outcomes, such as pre-term birth, large for gestational age babies, fetal defects, congenital anomalies, and perinatal death. Length of hospital stay was also reported as an adverse outcome of maternal obesity[7].

Most published studies on the effect of obesity on pregnancy outcomes have focused on primarily homogenous regional populations that are not ethnically diverse[8], but some researchers have shown that ethnic differences can have an impact on the association between obesity and adverse pregnancy outcomes[9]. This impact is particularly relevant for countries like Qatar, which has a diverse, multiethnic, transient population. The 2012 World Health Organization (WHO) STEPwise approach to Surveillance survey for Qatar showed that 68.3% of adult females were overweight and 43.2% were obese[10], highlighting the significance of the maternal obesity problem in the country. The public health care system in Qatar is broken down into primary and secondary/tertiary care systems, with primary care administered by the Primary Health Care Corporation (PHCC), and secondary/tertiary care administered by the Hamad Medical Corporation (HMC). Both systems classify pregnancies as high-risk when the mother is obese Class III or higher (body mass index [BMI] $\geq$40 kg/m^2), has a pre-existing medical condition, and/or obstetric complications, as per the guidelines of the Ministry of Health. Women with high-risk pregnancies

are directly referred to dedicated antenatal clinics of the HMC for specialized management. However, women with a BMI <40 kg/m^2, but who are still overweight or obese, are cared for through the PHCC; they are referred to the HMC only if they develop complications or for delivery.

Population attributable fractions (PAFs) are used to identify the burden of risk factors for a disease or condition in a given population[11]. Few studies have looked at PAFs of maternal obesity [12]. Obesity is highly prevalent in Qatar, hence it is critical to study PAFs associated with obesity in different ethnic groups to quantify the burden of disease that can be attributed to obesity, and thereby help develop targeted management strategies. We aimed to identify the impact of pre-pregnancy maternal BMI on adverse pregnancy outcomes in a low-risk, multi-ethnic population, and to calculate related PAFs.

Methods

The PHCC Database is linked to the Birth Register of Qatar; it includes information on all PHCC visits, and thus includes pre-pregnancy and maternal characteristics (e.g., age, nationality, pre-existing conditions), and pregnancy and neonatal outcomes. For this retrospective cohort study, we used the PHCC Database to identify all nulliparous women with singleton pregnancies who had their first antenatal visit at a PHCC facility between 1 June 2016 and 1 March 2017 and their pregnancy outcome at a HMC facility before 10 November 2017 (n=1245). The follow-up care for the mother and child initially happens at HMC and may then refer back to PHCC, however, this follow-up care was outside the scope of our study. We wanted to target women with low-risk pregnancies as defined by the Ministry of Health of Qatar. Therefore we excluded women with high-risk pregnancies, i.e., those with a pregnancy outcome prior to 24 weeks of gestation (n=8), those who were obese Class II and higher (BMI $\geq$35 kg/m^2, n=80), or who were under the age of 18 at their first antenatal visit (n=23). Women who gave birth to babies with indeterminate sex (n=2), or who experienced still birth (n=3), fetal death (n=4), or neonatal death (n=1) were also excluded. Among the exclusions were 10 women who met more than one exclusion criterion; therefore, the final study sample consisted of 1,134 women. The anonymized data used in this study was provided after the approval of the study by the research section of the PHCC (reference number PHCC/RS/17/07/007) and the Institutional Review Board (IRB) of Qatar University (Reference **QU-IRB 846-E/17**).

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Patient and Public Involvement

This study involved secondary analysis of data collected by PHCC during its routine interactions with the patients. No additional patient or public contact was undertaken in this study.

Maternal ethnicity

Included women were of 50 unique nationalities, and maternal ethnicity was categorized as Arab or non-Arab based on nationality. Women were designated as Arab if they were citizens of one of the 22 countries included in the list of League of Arab States (LAS)[13]. Our Arab study women came from 18 of these countries (Algeria, Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Sudan, Syria, Tunis, United Arab Emirates, and Yemen). The LAS have a common language (Arabic) and share a number of cultural, social, and dietary habits which may put them at different lifestyle and obesity-related risks as compared to non-Arabs. Women of other nationalities were designated as non-Arabs.

Pre-pregnancy body mass index

Pre-pregnancy BMI was calculated based on information recorded at the most recent pre-pregnancy visit available in the Primary Health Care Center Database. If this primary care visit was prior to 12 weeks from the date of the first antenatal visit, the BMI was treated as missing. Pre-pregnancy BMI was categorized as normal weight (BMI <25 kg/m^2) overweight (BMI 25-29.99 kg/m^2), and obese (BMI ≥30) based on standard WHO guidelines[14]. However, different BMI cut-offs were applied to Asians (n=405, overweight: BMI 23-27.5 kg/m^2; obese: BMI ≥27.5 kg/m^2), as recommended by the WHO expert consultation[15]. Sensitivity analyses, the results of which are not presented in this manuscript, showed that our application of different BMI cut-offs for Asians was valid, as using standard cut-offs underestimated the risk in that population.

Adverse pregnancy outcomes, adverse neonatal outcomes, and risk factors

Investigated adverse pregnancy outcomes included GDM, pregnancy-induced hypertension (PIH), preeclampsia, preterm delivery, assisted vaginal delivery, and caesarean section. Investigated adverse neonatal outcomes included macrosomia, large for gestational age, small for gestational age, neonatal intensive care unit referrals, and Apgar score <7 at 1 minute. Risk factors considered included maternal age, maternal ethnicity, and pre-existing conditions such as diabetes mellitus type 1 or 2, hypertension, and thyroid conditions. Retrospective review of patient medical records including doctors' notes were used to identify pre-existing conditions and most adverse outcomes such as GDM. Diagnosis of macrosomia, LGA and SGA was based off of the Weight Percentiles Calculator available from the WHO website[16 17].

Statistical analysis

Maternal characteristics and risk factors were tabulated using the observed data, and differences in the demographics across BMI categories were compared using Pearson's chi squared test. Thereafter, as pre-pregnancy BMI was not available for 101 (8.9%) of the study subjects, multiple imputation was performed to assign these values, with the underlying assumption that BMI values were missing at random[18 19]. Univariate and multivariate associations between maternal BMI category and adverse pregnancy and neonatal outcomes were assessed by logistic regression, using the imputed dataset.

Known and potential risk factors such as maternal age at first antenatal visit, pre-existing diabetes mellitus type 1 or 2, pre-existing hypertension, and pre-existing thyroid conditions were included as covariates in the final model. Maternal ethnicity was assessed as potential risk factor

while computing adjusted odds ratios (ORs) for associations between BMI category and adverse pregnancy and neonatal outcomes. Subgroup analysis was conducted by computing crude and adjusted ORs for adverse pregnancy and neonatal pregnancy outcomes separately for Arab and Non-Arab mothers.

The adjusted ORs were used to compute PAFs of overweight and obesity for Arab and non-Arab mothers. PAFs were used to estimate the proportion of adverse pregnancy and neonatal outcomes that could be prevented if either one of two scenarios were true[20]: 1) if overweight and obese women were all of normal weight before pregnancy; 2) if overweight and obese mothers had a one-category drop in BMI before pregnancy (i.e., obese to overweight, and overweight to normal weight). Scenario 0 was denoted the reference scenario, i.e., the current population as represented by the data. These scenarios were also analysed by ethnicity.

PAFs and corresponding 95% confidence intervals (CIs) were computed using a user-written procedure (punaf) in the Stata software[20]. All analyses in this research report were performed using the Stata 15[21] software package and Microsoft Excel. The significance level for this study was set at 5%, so p-value ≤0.05 was considered statistically significant.

Results

In our study sample, 86.33% of women were aged 18-30 years and 59.17% were of Arab ethnicity. The study sample included women from 50 countries, representing an extremely diverse data set. The most common risk factor among obese women was pre-existing thyroid conditions (5.22%).

Term deliveries (gestational age 37-41 weeks) accounted for 89.77% of births in the study sample (Table 1a).

==Insert Table 1(a) here ===

GDM was the most common adverse pregnancy outcome and was observed in 35.89% of the study sample, followed by cesarean section (24.96%). Preeclampsia was observed in 3.44% of the study sample. The prevalence of GDM, cesarean section, and preeclampsia increased with increasing BMI category (Table 1b).

== Insert Table 1(b) here ==

Obese Arab mothers had statistically significant, higher odds of developing GDM (adjusted OR=2.41, 95% CI 1.51–3.84, p <0.01) when compared to normal-weight Arab mothers. Although the odds were higher for obese non-Arab mothers when compared to their normal-weight counterparts (adjusted OR=1.58, 95% CI 0.96–2.62, p=0.07), these odds were not as high as those observed for Arab mothers, and the association was not statistically significant. Obese non-Arab women showed significantly higher odds (adjusted OR=3.83, 95% CI 0.98–15.00, p=0.05) of developing preeclampsia when compared to normal-weight non-Arab women. Finally, the odds of caesarean section were significant among overweight Arab mothers, as compared to their normal-weight counterparts (adjusted OR=1.57, 95% CI 1.00–2.48, p=0.05), but this association was not significant among obese Arab mothers or among obese non-Arab mothers when compared to their normal-weight counterparts (Table 2). Although higher odds were observed in obese (Figure 1)and overweight (Figure 2) mothers in both ethnic groups, p-values were not statistically significant for most adverse pregnancy or neonatal outcomes when compared to normal-weight counterparts.

==Insert Table 2 here===

== Insert Figure 1 here==

== Insert Figure 2 here==

Population attributable fractions

For preeclampsia, a one-category reduction in BMI among Arab mothers corresponded to a PAF of 46.28% for obese women and 38.61% for overweight women (Figure 3). For PIH, a one-category drop in BMI for obese women corresponded to a PAF of 50.83%, meaning that 50.83% of PIH cases could be avoided if obese mothers reduced their BMI category to overweight (Figure 3). Corresponding PAFs for neonatal outcomes were 65.23% for macrosomia and 30.42% for Apgar score <7 at 1 minute. Some of the CIs and PAFs were negative (e.g., small for gestational age and assisted vaginal delivery), indicating a protective effect of obesity on these outcomes, which means that removing obesity could increase these risks (Tables 3 and 4).

== Insert tables 3 and 4 here ==

For GDM, a one-category reduction in BMI corresponded to a PAF of 24.72% and 24.58% for obese Arab and non-Arab mothers, respectively (Figure 3). The PAF for macrosomia if all women were of normal weight before pregnancy was 13.73% for non-Arab women, and 6.78% for Arab mothers (Figure 4). The PAFs for neonatal outcomes after a one-category reduction in BMI are not shown in the Figure 3 and Figure 4, as they are mostly negative due to the small number of cases.

=== Insert Figures 3 and 4 here ==

Discussion

Our study confirms that there is an association between pre-pregnancy maternal BMI and adverse pregnancy and neonatal pregnancy outcomes in multi-ethnic populations, using adjusted ORs and PAFs. Previous studies have shown similar strengths of association between overweight and obesity and GDM[22], PIH[22 23], preterm delivery[12 24], assisted vaginal delivery[22 25], caesarean section[22 25], macrosomia[12], large for gestational age[24] and small for gestation age[24 25]. However, the present study found much higher ORs for preeclampsia in non-Arab mothers. This could be attributed to the large portion of Asian mothers in the non-Arab group, who have been reported to be susceptible to preeclampsia[26].

Our results confirm those of a recent study on nulliparous women in Qatar, which reported a higher incidence of GDM, caesarean section, and PIH in obese women[27], whereas overweight women were reported to have higher caesarean section rates only[27]. However, the overall incidence of these outcomes was much lower than in our study sample (GDM: 15% vs 35.89% in our study sample; caesarean section: 16% vs 24.98%). These difference cannot be explained by the data alone, since the earlier study[27] was carried out in a tertiary care setting, whereas this research focused on primary care settings.

The PAFs we report are much higher than those from some published studies[12], due to the high prevalence of overweight and obesity (i.e., exposure) in our study sample. Preeclampsia stands out, as any reduction in BMI category yielded a substantial reduction in the burden of this condition. A one-category reduction in BMI showed a much higher possibility of disease reduction among obese women than among overweight women, whether they were Arab or non-Arab. However, caesarean section was an exception to this trend, and showed a lesser PAF for a one-category reduction in BMI among obese women than overweight women. This can be explained

by the higher OR for caesarean section in overweight women as compared to obese women in both ethnic groups. It should be noted that a causal relationship between exposures and outcomes is generally assumed in PAF calculations. However, this relationship may not necessarily exist, and PAFs should be considered accordingly.

Unlike other reports, the exposure variable in our study was not self-reported. We used standard WHO recommended BMI cut-offs, except in the Asian population, in which Asian-specific cut-offs were applied. Results of a sensitivity analysis indicated that the use of these Asian-specific cut-offs is indeed clinically important in multiethnic populations. Indeed, Asian mothers must be classified as overweight and obese using the WHO-recommended cut-offs for Asians, otherwise high-risk patients may not be properly identified during antenatal care.

Patient nationality was used as a surrogate for ethnicity, but it is common for people to change their citizenship through immigration, which could have limited the strength of the conclusions of this study. However, a detailed analysis of nationalities revealed that the number of patients claiming citizenship to countries that are most likely targets for migrants was minimal (Canadians=0, Australians=0, Americans=3, British=1, French=1). Therefore, the use of nationality as a surrogate for ethnicity is reasonable and valid for this dataset.

Other reports from Qatar showed higher rates of conditions such as diabetes mellitus and cardiovascular diseases, which were not reflected in our study. These low rates may represent an information bias which did not allow us to properly adjust for potential confounders. Data on socioeconomic status and health center location were not available; hence it is not possible to attribute missing values to these factors or to any other variables for which data was not available.

GDM, preeclampsia, and cesarean section were significantly associated with pre-pregnancy BMI among our overweight and obese mothers, who are not generally considered to have at-risk pregnancies by the health care system in Qatar. High prevalence of GDM in normal-weight mothers (29.21%) indicates that BMI alone cannot explain the problem, which is instead related to population norms and characteristics. High risk of preeclampsia in overweight and obese mothers, especially among non-Arabs, indicates that early screening and management of hypertensive disorders is needed for this group. This implies that clinical screening is indicated for all mothers regardless of their pre-pregnancy BMI or ethnicity, preferably at the start of pregnancy.

The rate of cesarean section was very high in our study sample (25%), especially considering that pregnancies in overweight and obese women are currently considered low-risk by the health care system in Qatar. The odds of cesarean section were uncharacteristically high and similar in overweight and obese mothers regardless of ethnicity. Clinical implications cannot be drawn from these results without properly separating the cesarean sections by their indications (medically necessary vs elective), which were not available in the study sample. Our findings of an association between pre-pregnancy maternal BMI and cesarean section may not properly represent the true nature of the outcome risk and exposure, and should therefore be interpreted with caution.

As has been mentioned in above paragraphs, the retrospective cohort nature of this study limited our ability to validate or verify the elements of the dataset and other potential confounders through additional patient contact. The anonymity of the data by design made it impossible to undertake such a follow up. The strength of our findings is therefore directly related to the strength of the dataset used. The number of missing values in the exposure

variable, the pre-pregnancy BMI, meant that we were unable to ascertain a direct relationship for those records. However, the impact of such was minimized by using the multiple imputation techniques. The PAFs were computed using the punaf user written extension for Stata software and manual calculations for such cannot be undertaken due to the computational complexity of the task.

Adverse pregnancy outcomes were attributable to maternal obesity for even low risk patients. This suggests that, in contrast to the existing PHCC protocol which focuses only on high-risk pregnancies for intervention, overweight and obese women in Qatar should also be targeted earlier in their pregnancy, preferably prior to getting pregnant. We observed ethnic differences in the risk of adverse pregnancy outcomes. Planning and prevention approaches at the pre-conception stage are needed to raise awareness and reduce the burden of these adverse outcomes on the health care system. There is a need for an ecological approach that addresses societal, cultural, and personal influences by promoting good health at all levels. A top-down approach would work best to formulate public health policy to combat the issues raised. A combination of these public health interventions can help achieve the WHO Non-Communicable Disease Targets for the Global Action Plan by 2025.

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Contributors Conceptualization, S.S. and U.N.; methodology, S.S. and U.N.; software, S.S.; validation, S.S. and U.N.; formal analysis, S.S.; investigation, S.S. and U.N; resources, S.S.; data curation, S.S.; writing—original draft preparation, S.S.; writing—review and editing, S.S. and U.N.; visualization, S.S. and U.N.; supervision, U.N. ; project administration, S.S.; funding acquisition, U.N.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethical approval was obtained from The Primary Health Care Corporation (Reference Number **PHCC/RS/17/07/007)** on October 3, 2017 and the Institutional Review Board (IRB) of Qatar University (Reference **QU-IRB 846-E/17**) on November 11, 2017.

Data availability statement The database analysed for this research include information on all antenatal visits to Primary Health Care Centres, between 1 June 2016 and 1 March 2017. Data can be obtained by request from the Primary Health Corporation in Qatar.

Provenance and peer review Not commissioned; externally peer reviewed.

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Table 1(a): Selected characteristics of the study sample by pre-pregnancy maternal body mass index (BMI) in Qatar (N=1134)

	Pre-pregnancy BMI category					
	Normal Weight (N=404)	Overweight (N=399)	Obese (N=230)	Missing (N=101)	Total (N=1134)	P-Value
Maternal Age (years)						**<0.001**
18-24	212(52.48%)	141(35.34%)	73(31.74%)	48(47.52%)	474(41.8%)	
25-30	157(38.86%)	195(48.87%)	114(49.57%)	39(38.61%)	505(44.53%)	
31-44	35(8.66%)	63(15.79%)	43(18.7%)	14(13.86%)	155(13.67%)	
Maternal Ethnicity						**0.005**
Arab	254(62.87%)	240(60.15%)	114(49.57%)	63(62.38%)	671(59.17%)	
Non-Arab	150(37.13%)	159(39.85%)	116(50.43%)	38(37.62%)	463(40.83%)	
Pre-existing Hypertension						
Yes	8(1.98%)	10(2.51%)	4(1.74%)	2(1.98%)	24(2.12%)	0.94
No	396(98.02%)	389(97.49%)	226(98.26%)	99(98.02%)	1110(97.88%)	
Pre-existing Diabetes Mellitus Type 1 or 2						
Yes	5(1.24%)	4(1%)	4(1.74%)	0(0%)	13(1.15%)	0.67
No	399(98.76%)	395(99%)	226(98.26%)	101(100%)	1121(98.85%)	
Pre-existing Thyroid Condition						
Yes	18(4.46%)	10(2.51%)	12(5.22%)	2(1.98%)	42(3.7%)	0.22
No	386(95.54%)	389(97.49%)	218(94.78%)	99(98.02%)	1092(96.3%)	
Gestational Age at Delivery (weeks)						
<37	32(7.92%)	40(10.03%)	28(12.17%)	10(9.9%)	110(9.7%)	0.60
37-41+6d	370(91.58%)	357(89.47%)	200(86.96%)	91(90.1%)	1018(89.77%)	
≥42	2(0.5%)	2(0.5%)	2(0.87%)	0(0%)	6(0.53%)	

Values shown as Number(%)
Chi^2 test was used to determine differences across the BMI categories
Fishers Exact test was used when cell count was <5

Table 1(b): Distribution of adverse pregnancy and neonatal outcomes by pre-pregnancy maternal body mass index (BMI) in Qatar (N=1134)

	Pre-pregnancy BMI category					
	Normal Weight (N=404)	**Overweight (N=399)**	**Obese (N=230)**	**Missing (N=101)**	**Total (N=1134)**	**P-Value**
Pregnancy Outcomes						
Gestational Diabetes Mellitus	118(29.21%)	140(35.09%)	108(46.96%)	41(40.59%)	407(35.89%)	**<0.001**
Pregnancy-Induced Hypertension	14(3.47%)	14(3.51%)	17(7.39%)	1(0.99%)	46(4.06%)	**0.038**
Preeclampsia	8(1.98%)	14(3.51%)	15(6.52%)	2(1.98%)	39(3.44%)	**0.013**
Preterm Delivery	32(7.92%)	40(10.03%)	28(12.17%)	8(7.92%)	108(9.52%)	0.21
Assisted Vaginal Delivery	66(16.34%)	62(15.54%)	40(17.39%)	11(10.89%)	179(15.78%)	0.831
Cesarean Section	80(19.8%)	107(26.82%)	69(30%)	27(26.73%)	283(24.96%)	**0.008**
Neonatal Outcomes						
Macrosomia	11(2.72%)	8(2.01%)	13(5.65%)	1(0.99%)	33(2.91%)	**0.034**
Large for Gestational Age	25(6.19%)	31(7.77%)	23(10%)	7(6.93%)	86(7.58%)	0.22
Small for Gestational Age	65(16.09%)	55(13.78%)	32(13.91%)	22(21.78%)	174(15.34%)	0.606
NICU referral	36(8.91%)	46(11.53%)	22(9.57%)	10(9.9%)	114(10.05%)	0.449
Apgar Score <7 at 1 min,	19(4.7%)	17(4.26%)	14(6.09%)	4(3.96%)	54(4.76%)	0.582

Values shown as Number(%)

Chi^2 test was used to determine differences across the BMI categories

Abbreviations: NICU, neonatal intensive care unit.

Table 2: Odds ratios (ORs) and 95% confidence intervals (CIs) of the association between adverse pregnancy and neonatal pregnancy outcomes and body mass index (BMI) category by ethnicity after multiple imputation (N=1134)

	Arabs			Non-Arabs		
	Prevalence	Adjusted OR (95% CI)	P-Value	Prevalence	Adjusted OR (95% CI)	P-Value
Pregnancy Outcomes						
Gestational Diabetes Mellitus						
Overweight	92(34.98%)	1.24 (0.84 – 1.82)	0.28	64(36.99%)	1.23(0.76 – 2.00)	0.40
Obese	66(51.97%)	2.38 (1.51 – 3.84)	**<0.01**	54(43.2%)	1.60 (0.97 – 2.65)	0.07
Pregnancy-Induced Hypertension						
Overweight	11(4.18%)	1.66 (0.63 – 4.38)	0.31	3(1.73%)	0.41 (0.11 – 1.61)	0.20
Obese	4(3.15%)	1.21 (0.34 – 4.31)	0.76	13(10.4%)	2.41 (0.93 – 6.327)	0.07
Preeclampsia						
Overweight	6(2.28%)	1.11 (0.33 – 3.71)	0.86	9(5.2%)	2.56 (0.66 – 9.97)	0.18
Obese	7(5.51%)	2.64 (0.81 – 8.65)	0.11	8(6.4%)	3.83 (0.98 – 15.00)	**0.05**
Preterm Delivery						
Overweight	26(9.89%)	1.26 (0.66 – 2.41)	0.48	18(10.4%)	1.22 (0.57 – 2.61)	0.61
Obese	14(11.02%)	1.35 (0.63 – 2.91)	0.45	17(13.6%)	1.69 (0.78 – 3.68)	0.18
Assisted Vaginal Delivery						
Overweight	38(14.45%)	0.94 (0.57 – 1.55)	0.82	28(16.18%)	0.87 (0.48 – 1.58)	0.65
Obese	20(15.75%)	1.01 (0.55 – 1.86)	0.97	22(17.6%)	0.97 (0.52 – 1.81)	0.93
Cesarean Section						
Overweight	66(25.1%)	1.57 (1.00 – 2.48)	**0.05**	51(29.48%)	1.05 (0.64 – 1.74)	0.83
Obese	32(25.2%)	1.46 (0.83 – 2.53)	0.20	45(36%)	1.43 (0.84 – 2.44)	0.19
Neonatal Outcomes						
Macrosomia						
Overweight	7(2.66%)	0.86 (0.30 – 2.42)	0.77	1(0.58%)	0.37 (0.04 – 3.39)	0.38
Obese	6(4.72%)	1.48 (0.49 – 4.48)	0.49	7(5.6%)	3.05 (0.77 – 12.06)	0.11
Large for Gestational Age						
Overweight	19(7.22%)	1.06 (0.53 – 2.14)	0.87	15(8.67%)	1.52 (0.61 – 3.79)	0.37
Obese	13(10.24%)	1.46 (0.66 – 3.20)	0.35	12(9.6%)	1.75 (0.70 – 4.41)	0.23
Small for Gestational Age						
Overweight	34(12.93%)	0.84 (0.49 – 1.43)	0.52	30(17.34%)	0.93 (0.52 – 1.67)	0.82
Obese	17(13.39%)	0.90 (0.44 – 1.82)	0.77	19(15.2%)	0.84 (0.44 – 1.60)	0.59
NICU referral						
Overweight	26(9.89%)	1.15 (0.63 – 2.11)	0.65	23(13.29%)	1.30 (0.64 – 2.64)	0.46
Obese	8(6.3%)	0.64 (0.26 – 1.55)	0.32	17(13.6%)	1.30 (0.61 – 2.77)	0.49
Apgar Score <7 at 1 min.						
Overweight	13(4.94%)	1.24 (0.53 – 2.92)	0.63	6(3.47%)	0.59 (0.19 – 1.80)	0.47
Obese	8(6.3%)	1.72 (0.66 – 4.46)	0.27	6(4.8%)	0.86 (0.30 – 2.48)	0.50

For each ethnic group, normal weight was considered the reference category (OR = 1) for calculating ORs.
All outcomes were adjusted for maternal age at first antenatal visit. In addition: pre-eclampsia for pre-existing diabetes, and pre-existing hypertension, preterm delivery for pre-existing comorbid conditions, assisted vaginal delivery for pre-existing comorbid conditions, caesarean section for pre-existing comorbid conditions, macrosomia for pre-existing diabetes, large for gestational age for pre-existing diabetes, and small for gestational age was adjusted for pre-existing diabetes and pre-existing hypertension.
NICU, neonatal intensive care unit.

Table 3: Population attributable fractions (PAFs) % and 95% confidence intervals (CI) of adverse pregnancy and neonatal outcomes by pre-pregnancy body mass index among Arab mothers

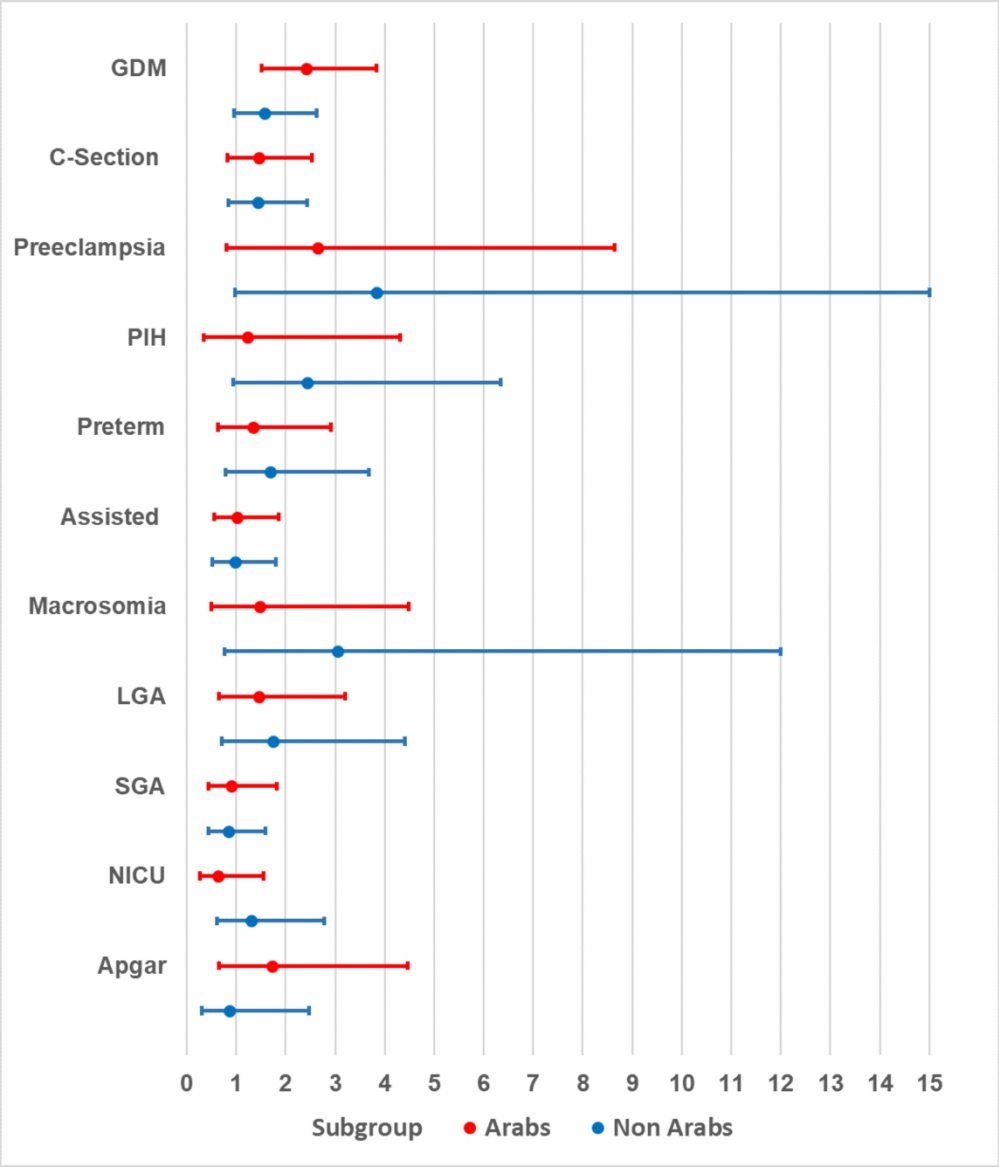
	All to Normal Weight (Scenario 1)	Obese to Overweight (Scenario 2)	Overweight to Normal (Scenario 2)
Pregnancy Outcomes			
Gestational Diabetes	13.64 (2.81 to 23.27)	24.72 (8.88 to 37.8)	12.52 (-7.28 to 28.66)
Pregnancy-Induced Hypertension	14.62 (-28.68 to 43.35)	**50.83 (1.46 to 75.46)**	-3.46 (-116.78 to 50.63)
Preeclampsia	**40.26 (-8.34 to 67.06)**	**46.28 (-8.98 to 73.52)**	**38.61 (-45.72 to 74.14)**
Preterm Delivery	15.04 (-11.09 to 35.03)	16.02 (-33.05 to 46.99)	18.14 (-28.65 to 47.91)
Assisted Vaginal Delivery	-3.11 (-22.13 to 12.95)	8.23 (-32.19 to 36.29)	-8.5 (-50.1 to 21.57)
Cesarean Section	14.09 (-0.9 to 26.86)	7.14 (-21.13 to 28.81)	19.24 (-5.27 to 38.03)
Neonatal Outcomes			
Macrosomia	6.78 (-47.09 to 40.91)	**65.23 (17.74 to 85.31)**	-44.54 (-257.57 to 41.58)
Large for Gestational Age	16.03 (-13.93 to 38.11)	22.26 (-29.92 to 53.48)	17.23 (-38.3 to 50.46)
Small for Gestational Age	-7.96 (-27.51 to 8.59)	-1.19 (-53.4 to 33.24)	-14.47 (-61.48 to 18.85)
NICU referral	7.91 (-18.08 to 28.18)	-25.28 (-104.33 to 23.18)	18.37 (-24.71 to 46.57)
Apgar Score <7 at 1 min.	1.67 (-37.59 to 29.73)	**30.42 (-38.63 to 65.08)**	-10.89 (-111.84 to 41.95)

Abbreviations: NICU, neonatal intensive care unit

Table 4: Population attributable fractions (PAFs) % and 95% confidence intervals (CI) of adverse pregnancy and neonatal outcomes by pre-pregnancy body mass index among non-Arab mothers

	All to Normal Weight	Obese to Overweight	Overweight to Normal
Pregnancy Outcomes			
Gestational Diabetes	16.2 (4.79 to 26.23)	24.58 (8.6 to 37.77)	12.18 (-7.12 to 28)
Pregnancy -Induced Hypertension	19.98 (-26.05 to 49.2)	**50.24 (1.25 to 74.93)**	-3.41 (-114.55 to 50.16)
Preeclampsia	**42.92 (-5.47 to 69.11)**	**46.42 (-9.27 to 73.73)**	**37.79 (-44.56 to 73.23)**
Preterm Delivery	16.89 (-10.67 to 37.59)	15.8 (-32.54 to 46.51)	17.86 (-28.14 to 47.34)
Assisted Delivery	-2.81 (-23.22 to 14.22)	8.14 (-31.83 to 36)	-8.27 (-48.48 to 21.06)
Cesarean Section	13.89 (-0.47 to 26.2)	6.48 (-18.95 to 26.47)	17.19 (-4.73 to 34.53)
Neonatal Outcomes			
Macrosomia	13.73 (-46.3 to 49.13)	**65.86 (17.93 to 85.8)**	-45.01 (-261.54 to 41.84)
Large for Gestational Age	18.86 (-13.59 to 42.04)	22.44 (-30.35 to 53.85)	17.29 (-38.52 to 50.62)
Small for Gestational Age	-8.73 (-30.31 to 9.27)	-1.13 (-50.1 to 31.86)	-13.69 (-57.58 to 17.98)
NICU referral	7.09 (-20.53 to 28.37)	-24.49 (-100.23 to 22.59)	17.79 (-23.81 to 45.41)
Apgar Score < 7	4.25 (-40 to 34.51)	**30.53 (-38.95 to 65.27)**	-10.93 (-112.38 to 42.06)

Abbreviations: NICU, neonatal intensive care unit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Subgroup
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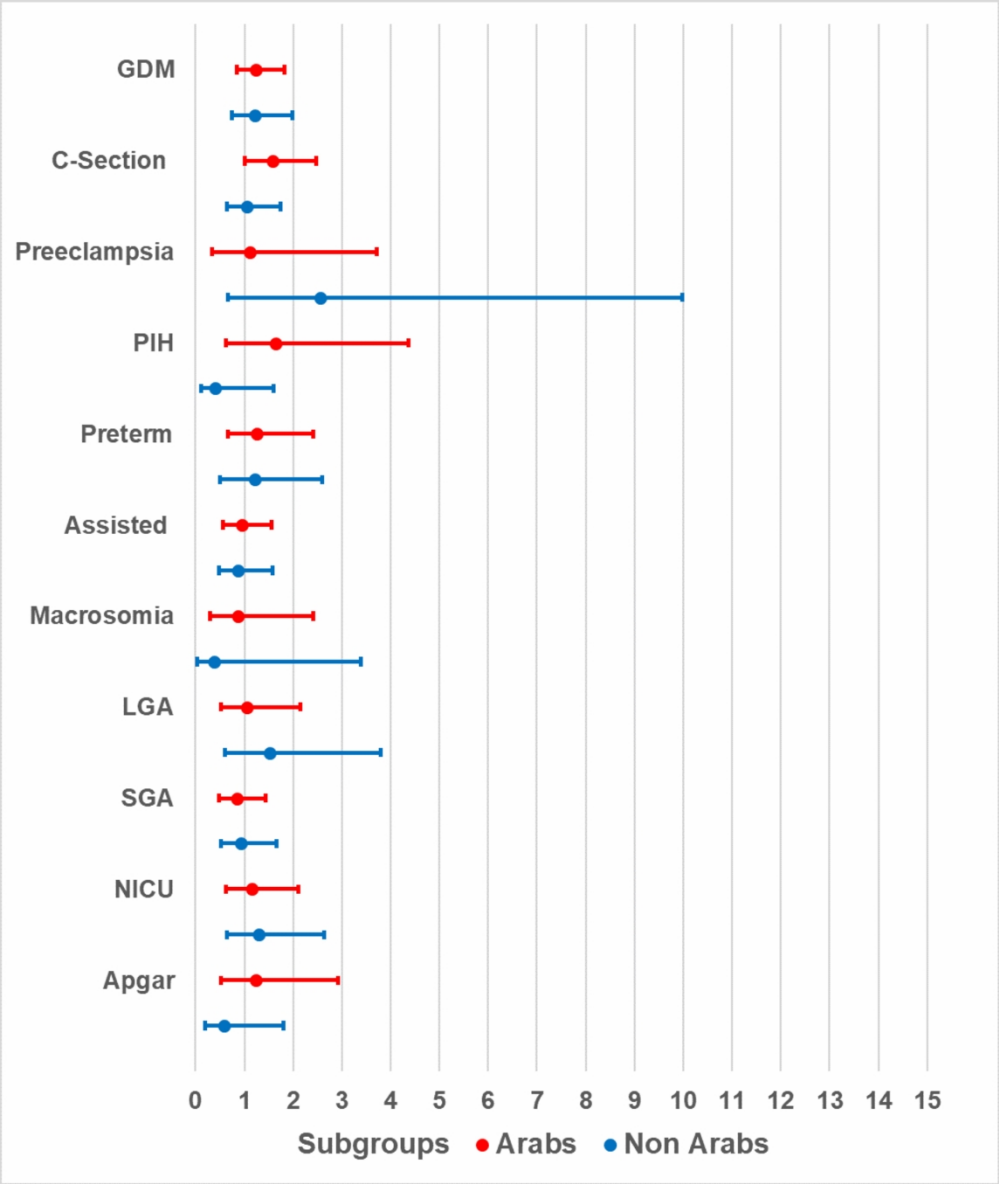
Non Arabs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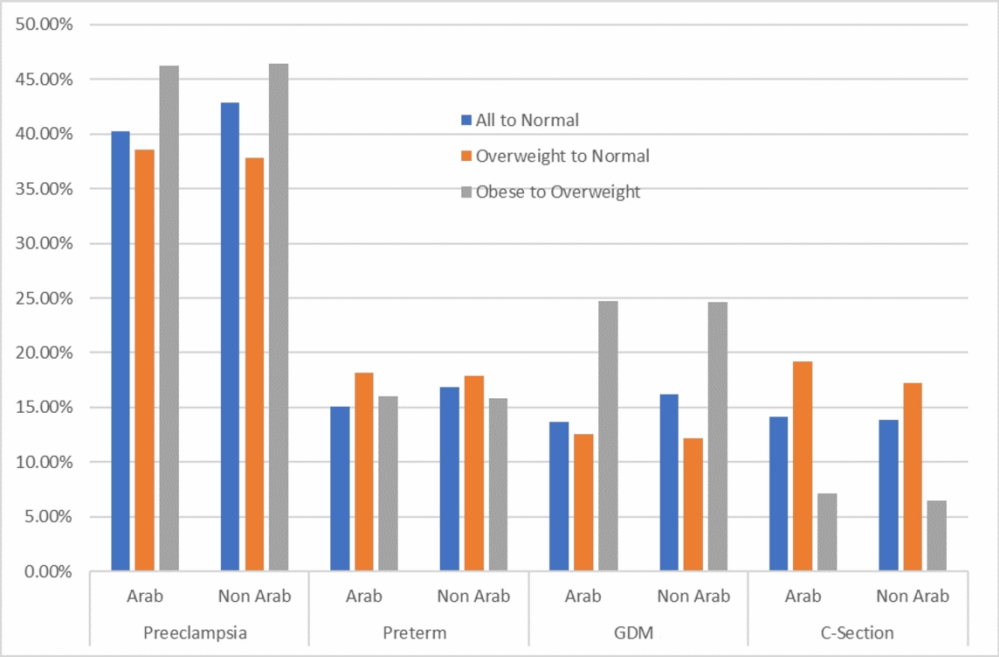
Non Arabs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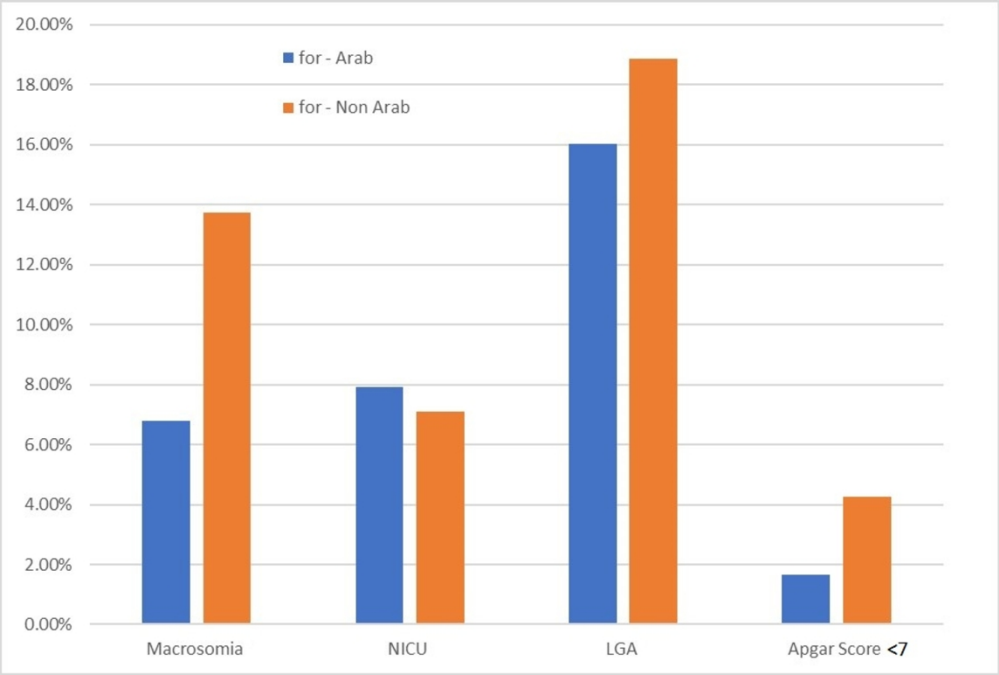
Non Arab
GDM
Arab
Non Arab
C-Section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for - Non Arab
Macrosomia
NICU
LGA
Apgar Score <7

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract Done, title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found Done, page 2
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Done, page 4
Objectives	3	State specific objectives, including any pre-specified hypotheses Done, page 4
Methods		
Study design	4	Present key elements of study design early in the paper Done, Abstract and page 6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Done, methods section, page 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up Done, methods section, page 6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable Done, methods section, page 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group Data source and methods of assessment of exposure and outcomes are presented in in the methods section page 6
Bias	9	Describe any efforts to address potential sources of bias Potential sources of bias are explained on page 13
Study size	10	Explain how the study size was arrived at All nulliparous women with singleton pregnancies who had their first antenatal visit at a PHCC facility between 1 June 2016 and 1 March 2017 and their pregnancy outcome at a HMC facility before 10 November 2017 (n=1245) were included in this study, methods section page 6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why All quantitative variables included in analysis with details of varaibles that have been categorized are presented in methods section page 6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding Done, all statistical methods to control for confounding on page 8-9
		(*b*) Describe any methods used to examine subgroups and interactions Done, multivariable logistic regression analysis and population attributable fractions were used to adjust for overweight and obesity for Arab and non-Arab mothers , pages 7-8

		(*c*) Explain how missing data were addressed Done, multiple imputation was used to handle missing data, page 8
		(*d*) If applicable, explain how loss to follow-up was addressed Not applicable
		(*e*) Describe any sensitivity analyses Sensitivity analysis was not applied
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed Done, methods section page 5
		(b) Give reasons for non-participation at each stage Done, page 5
		(c) Consider use of a flow diagram Flow diagram was not needed
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Done, table 1 and results section page 9-10
		(b) Indicate number of participants with missing data for each variable of interest Done, table 1, results page 9
		(c) Summarise follow-up time (eg, average and total amount) Not applicable
Outcome data	15*	Report numbers of outcome events or summary measures over time Not applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Done, tables 2,3, 4, and results section, pages 10-11
		(*b*) Report category boundaries when continuous variables were categorized Done, page 7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses Done, pages 9-10
Discussion		
Key results	18	Summarise key results with reference to study objectives Done, 12-15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Done, page 13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Done, pages 14-15
Generalisability	21	Discuss the generalisability (external validity) of the study results Done, page 15
Other information		

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Done, funding statement is presented after discussion

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.