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Pre-pregnancy maternal obesity in Greece: A case–control analysis

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ABSTRACT

Background—aims: Pre-pregnancy obesity may cause significant health implications for both mother and neonate. Our study aims to investigate the association between pre-pregnancy Body Mass Index and the risk for cesarean section, admission to Neonatal Intensive Care Unit, macrosomia and preterm delivery, in a Mediterranean country.
Study design: A matched retrospective case control analysis was conducted.
Subjects: The study population included all pregnant women (with known Body Mass Index data) who gave birth in the University Hospital of Patras between 1st of January 2003 and 31st of December 2008.
Outcome measures: Cases were defined as obese (338) or overweight (826) women.
Results: Overweight and obese women were at higher risk for cesarean section, NICU admission and preterm delivery ($\chi^2(2) = 36.877$, $p < 0.001$, χ^2 Imes and Burke (2014) $= 6.586$, $p = 0.037$ and χ^2 Imes and Burke (2014) $= 7.227$, $p = 0.027$ respectively). Neonatal mean birthweight was higher among obese and overweight women ($p < 0.0001$).
Conclusions: Both obese and overweight pregnancies should be considered as high risk pregnancies, due to more frequent adverse pregnancy outcomes (cesarean delivery, preterm delivery and NICU admission).

1. Introduction

Obesity is a pandemic in the 21st century. According to World Health Organization, more than 1.9 billion adults were overweight and obese in 2008, and according to estimates, obese adults will surpass 1.12 billion in 2030 (20% of adult population worldwide). This increase in obesity rates, will be more rapid in developing countries [1].

Obesity has been recognized as a risk factor for metabolic syndrome, diabetes mellitus, coronary heart disease, thromboembolism, obstructive sleep apnea, cancer (colon, breast, cervical) and depression [2].

Pre-pregnancy obesity varies worldwide from 1.8% to 25.3%. In USA, it ranges from 18.5% to 38.3% [3]. In Europe, it is estimated that one in five pregnant women is obese [4]. Central, Eastern and Southern Europe come first in prevalence of overweight and obesity [5]. Maternal BMI was found to increase over the years, in Europe; however, its prevalence differs between different countries [6].

During the last decade, obesity in Mediterranean countries rise in an alarming rate [7]. In Eastern Mediterranean, the obesity rates in women are among the highest worldwide (35–75%) [8]. INMA study in Spain and RHEA study in Greece found that overweight and obese mothers reached 18% and 8%, respectively, in Spain and 20% and 11%, respectively, in Greece [5].

Pregnancies by obese women, are at high risk for adverse outcomes in both mother and neonate. More precisely, maternal obesity has been associated with maternal comorbidities (gestational diabetes, preeclampsia, thromboembolism), delivery complications (preterm delivery, trauma, cesarean delivery, placental pathological lesions) [9] and neonatal comorbidities (macrosomia, low Apgar score, NICU admission) [10].

To our knowledge, there are very few studies focusing on pregnancies in Mediterranean population, investigating pregnancy outcome in overweight and obese women. The aim of this study, therefore, was to evaluate the effect of pre-pregnancy obesity, on the mode of delivery, preterm delivery and neonatal morbidity in a Mediterranean country.

2. Materials and methods

2.1. Study population

We conducted a retrospective case control study, in the region of Western Greece, which is a distinct geographical area with a population of 680,000 inhabitants containing Patras City as a capital and many surrounding rural communities. All available data from University Hospital of Patras (UHP) which is the largest hospital in Western Greece, serving more than 500,000 people, was used. From 2003 to 2008, 39,648

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deliveries occurred in Western Greece [11]. All deliveries of living neonates between 1st January 2003 and 31st December 2008, which took place in Department of Obstetrics (UHP), were included in our study. Fetal and perinatal losses were excluded.

In our analysis, case group included any pregnant woman of the Department of Obstetrics, whose BMI before pregnancy was equal or over 25. Control group included any pregnant woman, whose BMI was between 18.5 and 24.99 before pregnancy. Controls were selected according to maternal age, maternal residence and the date of the labor.

In our analysis, cases (obese or overweight women) were compared to controls in four categories:

a. Mode of delivery (cesarean section vs vaginal delivery)
b. Neonatal Intensive Care Unit (NICU) admission
c. Mean birthweight—macrosomia
d. Preterm delivery (<37 weeks)

Women with diabetes mellitus (type 1, 2 or pregnancy induced) and hypertension disorders were excluded.

2.2. Data collection

Data were collected from hospital records, based on obstetric and neonatal notes. Women's weight and height were measured in the first visit in the Department of Obstetrics (between 4 and 12 weeks) by an experienced nurse. Pregnant women were recommended to undergo a glucose tolerance test (planned in the outpatient Department) between 24 and 26 weeks of gestation (or earlier if there was a medical history of diabetes mellitus). In every monthly visit, blood pressure was measured. Urine analysis to check for proteinuria was made in the first visit and every month thereafter until delivery.

Additional information regarding the maternal medical and obstetrical history was derived from women's files as well. Specifically, demographic data (age, ethnic group, marital status, and contact details), medical history data (height and pre-pregnancy BMI, comorbidities, if any), obstetrical history (gravida, parity, complications in previous pregnancies either pre- or postnatal, and contraception methods) were documented. Furthermore, gestational age at delivery, mode of delivery and indications for cesarean section or assisted vaginal delivery, as well as neonatal data (birthweight, sex, NICU admission, perinatal mortality and morbidity rates) were recorded.

2.3. Definitions

According to World Health Organization, maternal BMI was categorized into three groups: less than 18.5 kg/m^2 (Underweight), 18.5–24.99 kg/m^2 (Normal), 25–29.99 kg/m^2 (Overweight), greater or equal to 30 kg/m^2 (Obese). Obesity was subcategorized into three subgroups: 30–34.99 kg/m^2 Obesity class I, 35–39.99 kg/m^2 Obesity class II, greater or equal to 40 Obesity class III—morbid obesity. Delivery of a living neonate in Greece includes the delivery of any fetus equal or over 23 weeks of gestation. Full term neonates were defined as neonates born at 37^{+0}–40^{+6} weeks of gestation. Preterm delivery is a delivery of a preterm neonate less than or equal to 36^{+6} weeks. Macrosomic neonates were those whose weight was equal or greater to 4000 g.

Emergency Cesarean Section was defined as any cesarean section that was performed for fetal distress, maternal reasons (e.g. preeclampsia, respiratory problems) or obstetrical reasons (e.g. placental abruption).

Assisted Vaginal Delivery was defined as any instrumental delivery (use of vacuum, forceps or both).

Neonatal Intensive Care Unit admission includes the admission of the neonate in the Unit, during the first 28 days of life.

Maternal residency was categorized into 4 groups: A. Cities – Capitals ≥100,000 population, B. Cities with population between 100,000–5000, C. Towns & Villages ≤5000 population and D. Islands.

2.4. Statistical analysis

For data analysis the numerical parameters were imported into Microsoft Excel 2010 and subsequently transferred to the Windows Statistical Package for Social Sciences (SPSS) 21.0 for statistical processing. Initially, we used descriptive and frequency statistics. Our study divided in three groups, where the statistical analysis was conducted: among the obese, the overweight (cases) and the women of normal BMI (controls). The differences among the obtained groups were determined by applying the Kruskal – Wallis test, a non-parametric method that is a non-parametric equivalent of a oneway analysis of variance, but unlike ANOVA does not assume a normal distribution of the residuals. Baseline characteristics were analyzed using either two-sample t tests or Wilcoxon rank sum tests for continuous data, and Chi-squared tests or Fisher's exact tests for categorical data were conducted after testing for normality. A significance level of 5% was used throughout the analysis. The incidence rates of adverse events were compared with the use of Fisher's exact tests.

3. Results

3.1. Population of the study

Between 1st January 2003 and 31st December 2008, 8293 birth records were recorded in the Department of Obstetrics in University General Hospital of Patras. Of those, 2536 were excluded for missing data (incomplete files). Additionally, 208 records were excluded as they referred to stillbirths, terminations of pregnancy and missed miscarriages. Finally 5549 pregnancies were included in our analysis. A case – control analysis was conducted (Table 2). There were 1164 cases included in the study (338 obese and 826 overweight), matched to 2328 controls (676 and 1652 women with normal BMI, respectively). Each obese case was matched to two controls (2:1 study) and each overweight case to four controls, according to age, region and year of delivery. Maternal and neonatal characteristics are presented in Table 1.

3.2. Mode of delivery

The risk of obese women, having cesarean section, was higher, compared to controls ($\chi^2(2) = 36{,}877$, $p < 0.001$). Emergency cesarean section, in women who undergone a cesarean section or assisted vaginal delivery in women who delivered vaginally, did not differ between cases and controls (data not shown). When women with diabetes mellitus and hypertension were excluded, obese subjects remained at increased risk of deliver by cesarean section compared to controls.

3.3. NICU admission

Offspring of obese mothers were at a times increased risk of NICU admission, compared to offspring of subjects with normal BMI ($\chi^2(2) = 6.586$, $p = 0.037$).

3.4. Mean birthweight

Neonatal mean birthweight in the obese group was higher compared to mean birthweight of neonates in the control group [3142 ± 645.81, 2993 ± 664.14 respectively, $p < 0.0001$].

3.5. Preterm delivery

The risk of preterm delivery (<37 weeks) was increased in the obese group, compared to controls ($\chi^2(2) = 7.227$, $p = 0.027$).

Table 1
Maternal and neonatal characteristics in cases and controls.

Maternal characteristics		Obesity cases (338)	Controls (A) (676)	Overweight cases (826)	Controls (B) (1.652)
Ethnicity	Greek	326 (96.4%)	620 (91.7%)	745 (90.2%)	1504 (91%)
	Albanian	8 (2.4%)	39 (5.8%)	59 (7.1%)	105 (6.4%)
	Roma	1 (0.3%)	5 (0.7%)	12 (1.5%)	16 (1%)
	Other	3 (0.9%)	12 (1.4%)	10 (1.2%)	27 (1.6%)
Age		41 ± 4.24	41 ± 1.41	37.73 ± 4.79	37.97 ± 5.13
Conception	Natural	313 (92.6%)	649 (96%)	783 (94.8%)	1593 (96.4%)
	IVF	20 (5.9%)	18 (2.7%)	31 (3.8%)	39 (2.4%)
	Other[a]	5 (1.5%)	9 (1.3%)	12 (1.4%)	20 (1.2%)
Delivery	Vaginal	134 (39.6%)	348 (51.5%)	399 (48.31%)	927 (56.13%)
	Cesarean	204 (60.4%)	328 (48.5%)	427 (51.69%)	725 (43.89%)
Geographic area	A	164 (48.5%)	328 (48.5%)	948 (57.4%)	442 (53.5%)
	B	87 (25.7%)	174 (25.7%)	434 (26.3%)	210 (25.4%)
	C	59 (17.4%)	118 (17.5%)	204 (12.3%)	125 (15.1%)
	D	23 (6.8%)	46 (6.8%)	41 (2.5%)	39 (4.7%)
Neonatal characteristics					
Birthweight[b]		3.470 ± 1.598	3.332.5 ± 590	3218 ± 580.07	3180 ± 532.9
Gestational age[b]		31.5 ± 13.435	33 ± 12.727	38.12 ± 1.96	38.31 ± 1.90
Sex	Boys	163 (48%)	357 (52.8%)	424 (51.3%)	869 (52.6%)
	Girls	174 (51.5%)	319 (47.2%)	402 (48.7%)	783 (47.4%)
	Unknown	1 (0.3%)	–	–	–
NICU admission		32 (9.5%)	58 (8.6%)	54 (6.54%)	95 (5.75%)
Prematurity (weeks)	<34	17 (5.03%)	30 (4.44%)	27 (3.3%)	44 (2.7%)
	34^{+0}–36^{+6}	36 (10.65%)	67 (9.91%)	69 (8.4%)	133 (8.1%)
	37^{+0}–37^{+6}	63 (18.6%)	103 (15.24%)	123 (14.9%)	203 (12.3%)
	38^{+0}–41^{+6}	217 (64.2%)	469 (69.38%)	603 (73%)	1259 (76.2%)
	Total	333	669	822	1639

[a] Intrauterine insemination or ovulation induction drugs.
[b] Mean ± standard deviation.

3.6. Mean birthweight—macrosomia

We found that there was not a statistically significant difference in macrosomia between the different groups ($\chi^2(2) = 5.066$, $p = 0.079$).

4. Discussion

The prevalence of maternal obesity and overweight demonstrated in our study was 6.1% (338) and 14.9% (826) respectively. To our knowledge, this is the first attempt to measure the burden of maternal obesity in a large population sample in Greece. Previous small studies, from northern Greece, have shown a higher prevalence of maternal obesity (up to 25.6%) [12]. Maternal pre-pregnancy obesity has been previously correlated to adverse pregnancy outcomes, for both mother and neonate [13].

In our case control analysis, a positive relationship between overweight and obesity and delivery by cesarean section was reported. There was a higher occurrence of cesarean section rates in both overweight and obese subjects, compared to controls. These findings are similar to the results of previous studies [14]. A possible explanation of these findings is based on adipose tissue's endocrine function. Adipose tissue produces hormones such as leptin, adiponectin and visfatin, which play a crucial role in metabolism, inflammatory response and mediating crosstalk between insulin dependent tissues. Hormone secretion in obese women differs to normal BMI women (adiponectin's secretion in obese patient is reduced, angiotensin and TNFa are produced and may cause high blood pressure and thrombosis respectively, leptin secreted from adipose tissue may influences placental secretion) and these alterations result in endothelial dysfunction. This could be responsible for adverse pregnancy outcomes such as preeclampsia and fetal distress, which are common causes of preterm delivery and/or delivery by cesarean section [15].

The cesarean section rate in our analysis was higher compared to the rates reported in other European countries – for similar periods – or

Table 2
Results of case–control analyses (A&B) and number of subjects included in the analyses.

	Analysis A (Obesity)	Diabetes mellitus and hypertensive disorders excluded	Analysis B (overweight)	Diabetes mellitus and hypertensive disorders excluded
Cesarean section (CS)	OR 1.98 CI 1.516–2.580 $p < 0.001$	OR 1.76 CI 1.337–2.310, $p < 0.001$	OR 1.37 CI 1.157–1.618, $p < 0.001$	OR 1.31 CI1.108–1.557 $p = 0.002$
Cases/controls	204/294		427/725	
NICU admission	OR 1.58 CI 1.00–2.550 $p = 0.06$	OR 1.4 CI 0.835–2.360 $p = 0.198$	OR 1.15 CI 0.811–1.618 $p = 0.439$	–
Cases/controls	32/42		54/95	
Macrosomia	OR 1.06 CI 0.591–1.910 $p = 0.840$	OR 1.14 CI 0.623–2.076 $p = 0.674$	OR 1.5 CI 1.044–2.167 $p = 0.027$	OR1.47 CI 1.008–2.135 $p = 0.044$
Cases/controls	18/34		53/72	
Preterm delivery[a]	OR 1.61 CI 1.094–2.354 $p = 0.015$	OR 1.46 CI 0.964–2.198 $p = 0.073$	OR 1.1 CI 0.840–1.424 $p = 0.50$	–
Cases/controls	53/71		96/177	

[a] ≤ 37 weeks of gestation.

worldwide, even in normal weight women [16,17]. This observation has been previously reported in Greece [18].

Neonates of overweight and obese mothers were at higher risk of being admitted to an NICU. However, our results were statistically significant in the obese group. Unfortunately, in our study, the indications for admission to an NICU were not reported. Nevertheless, the increased morbidity (jaundice, hypoglycemia, birth defects, congenital anomalies) of neonates of overweight and obese women has been previously reported, which is probably the main reason that could explain this phenomenon [13].

In both groups, obese and overweight, an increased risk of a higher mean birthweight in neonates of obese and overweight subjects has been reported. This could be explained, as neonates of obese and overweight mothers have higher levels of glucose, which pass through the placenta and attribute to greater fetal growth (hyperglycemia, hyperinsulinemia). There is a tendency towards obese mothers to have a macrosomic neonate; however, these results did not show statistical significance probably due to small sample (data not shown). In recent studies, a positive correlation between obesity and macrosomia, has been demonstrated [19]. In our study this relationship did not reached statistical significance. Although previous studies show a positive relationship between overweight women and neonatal macrosomia [20], other studies found no statistically significant difference for this relationship [21].

Preterm delivery rates in pregnancy complicated by obesity have been investigated in the literature with conflicting results. Many researchers have found a positive correlation between overweight, obesity and preterm delivery [22], while others do not support this correlation [23]. Our data demonstrated a positive relationship between obesity and preterm delivery. The causes of this observation are not clearly understood. However, endothelium dysfunction that was mentioned above may influence maternal–fetal homeostasis and may result to reduced blood flow to the fetus. This may be the first step in sequence of reactions causing preterm birth.

To enforce our correlations, women with diabetes mellitus and hypertensive disorders, were excluded from our case control analyses. After the exclusion, the same analysis was conducted in these new groups. Diabetes and hypertension could have been confounding factors for our correlations. Many researchers have found diabetes as a risk factor for cesarean section in obese women [24]. Moreover, maternal diabetes increases the risk of neonatal macrosomia [25]. Even if the pregnant woman has a good glycemic control, the prevalence of macrosomia remains in high levels [26]. Additionally, neonates of diabetic mothers are at higher risk of being admitted to an NICU. It has been suggested that 8–10% of neonates of diabetic mothers were admitted to an NICU admission because of hypoglycemia and perinatal distress [27].

Almost 10% of pregnancies are complicated by hypertensive disorders [28]. Similar to diabetes, hypertension disorders have been correlated to preterm delivery, placental abruption and post-partum hemorrhage [29]. A higher risk of cesarean section [30] and NICU admission has been reported in women with preeclampsia and their offspring [31].

In the second case control analysis, after the exclusion of diabetes and hypertensive disorders, overweight and obese women were at higher risk of cesarean section. Additionally, neonates of overweight women were at increased risk of macrosomia.

Future research should include multi center prospective trials that could further stratify the risks not only according to maternal prepregnancy BMI but to maternal diet and glycemic control as well.

4.1. Strengths and limitations

To our knowledge this is one from the first studies focusing on overweight and obesity before pregnancy in a Mediterranean population in a large study sample. In order to exclude confounding factors, a second case control analysis was conducted with the exclusion of patients with diabetes mellitus and/or hypertension.

The limitations of our study include data collection limitations. Unfortunately, maternal prepregnancy BMI data were missing in 2536 subjects (30%). However, in this sample maternal age, residency, mode of delivery, neonatal admission to NICU, macrosomia and prematurity did not differ from our study population (data not shown). Another limitation of our study was that the causes of preterm delivery were not reported. Therefore, we could not evaluate the incidence of Premature Rupture of Membranes (PPROM) or other possible causes of preterm delivery (infection, maternal comorbidities, Intrauterine Growth Restriction – IUGR – etc.). Additionally, indications for NICU admission were not measured in our study. For this reason, any possible tendencies towards specific complications of the neonate (infection, anomalies, congenital defects etc.) were missed.

The results of our case control retrospective study confirm that increased BMI (with the mother being either overweight or obese) is associated with adverse pregnancy outcomes (cesarean section, NICU admission, neonatal macrosomia and preterm delivery). Counseling women about pre-pregnancy weight loss and balanced weight gain during pregnancy could be beneficial for these high-risk pregnancies.

5. Conclusion

This study showed obesity as an independent risk factor for adverse pregnancy outcomes regarding cesarean section, NICU admission, macrosomia and preterm delivery. The risk is also high for overweight subjects.

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Contribution to authorship

E. Papachatzi was responsible for data acquisition and manuscript preparation.

S. Paparrodopoulos was responsible for data interpretation and statistical analysis.

V. Papadopoulos was responsible for conception and study design.

G. Dimitriou was responsible for critical revision of the manuscript.

A. Vantarakis was responsible for conception and manuscript preparation.

Details of ethics approval.

The study was approved by the hospital's ethics committee (Number 2/19-02-2013 signed form).

Conflict of interest

The authors declare no conflict of interest.

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