Maternal obesity, neonatal morbidity, and mortality, Southeast Metropolitan Health Service, Chile, 2014-2018. A retrospective pregnancy cohort study

*Oméga Chéry[1], Paula Bedregal[2], Gonzalo Valdivia[2], Vanessa Jaelle Dor[1], Oslando Padilla[2]

Author affiliations: [1]FETP, Haïti; [2]Pontifical Catholic University of Chile

*Corresponding author: Dr. Oméga Chéry, Direction d'Épidémiologie, des Laboratoires et de la Recherche (DELR), Ministère de la Santé Publique, Port-au-Prince, Haiti.Email: omega.chery@yahoo.fr / cheryomega@gmail.com

Abstract

Introduction

The prevalence of obesity continues to grow over the years. Maternal obesity is an established risk factor for mothers and newborns. We aimed to study the relation between maternal obesity, neonatal morbidity, and mortality.

Population and Methods

We conducted a retrospective cohort study in Santiago's Southeast Metropolitan Health Service 2014-2018 birth database, Chile, including 19,946 mothers and their newborns. We used data on sociodemographic variables, nutritional status at the beginning and during pregnancy, and maternal morbidity. We assessed several birth, perinatal, and neonatal health outcomes. We estimated means, frequencies, and risk and odds ratios (OR), using a two-sided *P*-value <0.05 to determine statistical significance. Multivariate logistic regression analysis controlled for potential confounding factors.

Results

The most common outcomes were fetal macrosomia (9.2%), and hospitalization (10.6%) while neonatal mortality (NM) was (5.2 ‰). Obesity at the beginning of pregnancy was 28.8%, and differed by maternal age, educational and socio-economic levels, and morbidity such as diabetes mellitus. Risk of NM (OR =1.5; 95% CI = 1.1 - 2.3) and fetal macrosomia (OR =1.7; 95% CI = 1.7 - 2.1) was higher in newborns of obese mothers. Excessive Gestational Weight Gain rate was associated with fetal macrosomia (OR = 1.8; 95% CI =1.6 - 2.0) and neonatal admission to emergency (OR = 1.2; 95% CI =1.1 - 1.4), but not with NM (*P*-value=0.265).

Discussion

Maternal obesity was found associated with adverse neonatal outcomes, findings that are biologically plausible. We recommend the promotion of maintaining a normal weight before pregnancy and an adequate gestational weight gain.

Key Words: Maternal obesity, obese, neonatal, mortality, morbidity, newborn, mother, gestational, weight, gain, Chile.

Suggested citation: Chéry O, Bedregal P, Valdivia G, Dor VJ, Padilla O. Maternal obesity, neonatal morbidity, and mortality, Southeast Metropolitan Health Service, Chile, 2014-2018. A retrospective pregnancy cohort study. *Am J Field Epidemiol* 2023; 1 (1):

Introduction

Obesity is one of the most critical public health problems worldwide, with increasing prevalence in many countries, and currently described as a pandemic [1-3]. It is defined as an abnormal or excessive accumulation of fat which is harmful to health [4]. Obesity is associated with increased morbidity, disability, and premature mortality from cardiovascular diseases, diabetes mellitus, ischemic heart disease, cancer, and musculoskeletal disorders [5].

The worldwide prevalence of obesity nearly tripled between 1975 and 2016, with over half of the adult population being obese or overweight, with a higher prevalence in women and men in the 30-40 years of age group, and with alarming predictions [6-8]. The prevalence is particularly high in the United States of America and Latin America and lower in Southeast Asia [9]. In Latin America obesity/overweight affects almost 60 percent of the adult population [10], and Chile ranks second in female obesity and third in male obesity in the subregion [11]. Obesity in Chile increased from 13.6% in 2003 to 34.4% 2016-7 [12].

Obesity increases in women of childbearing age and during pregnancy worldwide [13-15], ranging in prevalence from 1.8% to 25.3% in different countries of the world [16]. In Chile 23.6% of women of childbearing age and 20.9% of pregnant women were obese between 2009-2010 [11,13].

Obesity presented during pregnancy, or maternal obesity, can be diagnosed at the beginning of pregnancy (at the first antenatal medical visit) [17] or identified as an excessive weight gain during pregnancy.

Maternal obesity is associated with metabolic inflammation, characterized by elevated adipose tissue and sustained systemic levels of pro-inflammatory cytokines and accumulation of macrophages in

adipose tissue [18-22]. Furthermore, these changes extend to the placenta, suggesting a potential fetal exposure to an inflammatory environment for fetal development [18]. In animal models, maternal obesity has been shown to induce fetal inflammation that can result in the promotion of adipogenesis and increased adiposity in the offspring [18-22]. Maternal obesity constitutes one of the most common high-risk obstetric syndromes, resulting on a number of complications during pregnancy [23].

Consequences of obesity during pregnancy extend beyond the woman, to her offspring. Newborns of obese mothers during pregnancy have more complications in the perinatal period such as fetal macrosomia, prematurity, congenital anomalies, low APGAR, neonatal intensive care unit requirement, hypoglycemia, meconium-stained amniotic fluid, abnormal heart rate patterns, fetal trauma during delivery and increased perinatal and neonatal mortality [3,13, 24].

Given the increasing prevalence of obesity in women of reproductive age, it is important to study its relation with neonatal morbidity and mortality in Chile, since even a modest association can have a considerable impact on the population. The present study assessed whether maternal obesity is associated with an increased risk of neonatal morbidity and mortality in the Southeast Metropolitan Health Service (SSMSO), in Santiago, Chile.

Population and Methods

The SSMSO is one of the six Chilean's healthcare public services in the metropolitan area of Santiago, Chile, for the southeastern communities of Puente Alto, La Granja, La Pintana, Pirque, and Maipo. SSMSO healthcare is provided by primary healthcare facilities networking with three secondary-level hospitals, La Florida, Padre Hurtado, San José de Maipo, and a tertiary-level hospital, Dr. Sótero del Río. This latter facility hosts the Information, Management and Analysis Unit (IMAU) that receives data from all the SSMSO facilities serving those five communities. The SSMSO IMAU's 2014-2018 birth database comprised 109,879 observations on newborns and their mothers of all delivered births at SSMSO facilities among residents of all the communities served by the SSMSO from 2014 to 2018, hence, constituting a population-based cohort representative of the SSMSO pregnant population, considered one of the most representative regions of Chilean population. Therefore, we submit that a cohort based on maternal and birth records data from SSMSO would likely be representative of most births in Chile.

We excluded records that did not include information on vital status of the newborn through the first 28 days of life, maternal height and/or weight control at the beginning of pregnancy or had inconsistent data on maternal height and pre-pregnancy weight. In addition, newborns with gestational age <22

weeks and / or birth weight <500 grams were also excluded from the analysis because of their extreme low survival. After all these exclusions the analytic dataset comprised 19,546 records for the study.

Main exposure of interest

Newborns whose mothers were obese at the beginning of pregnancy or had excessive weight gain during pregnancy were considered as exposed, while newborns whose mothers were neither obese at the beginning of pregnancy nor had excessive weight gain during pregnancy were considered unexposed. Thus, maternal obesity (obesity at the beginning of pregnancy or excessive weight gain during pregnancy) represent the main exposure.

Outcome variables

Neonatal morbidity and mortality were the main outcome variables. Neonatal morbidity included the following: preterm and post-term birth, low birthweight, fetal macrosomia, neonatal sepsis, admission to the emergency department, hospital admission, and length of the hospital stay.

Statistical analysis

We calculated absolute and relative frequencies for categorical variables and measures of central tendency and dispersion for continuous variables. We described the newborns according to perinatal and neonatal characteristics, and their mothers according to their nutritional status at the beginning and during pregnancy and by sociodemographic profile, obstetric history, and chronic morbidity (diabetes mellitus, high blood pressure, hypothyroidism, drug addiction) prior and during pregnancy.

We compared proportions and averages between exposed / unexposed to maternal obesity within newborns with and without neonatal morbidity and mortality to identify differences between both groups and measured the association between maternal obesity and neonatal mortality, and morbidity by calculating the prevalence at birth risk or relative risk (RR) and / or mean difference ($\bar{x}$ diff.).

Different statistical tests were used to corroborate the association between the outcome and exposures of interest variables. We used the Pearson's chi-square, Fisher's exact or Yates’s correction to statistical testing when comparing proportions. For polytomous categorical variables, we used the Cochran-Armitage chi-square test to assess trends of neonatal morbidity and mortality across levels of exposure. We used the Student's t-test for independent samples to compare averages between continuous variables of two categories. We used a two-sided *P*-value <0.05 to determine statistical significance. Potential confounding variables were assessed through stratified and multivariate analysis with logistic regression, calculating crude and adjusted Odds Ratio (OR and ORa, respectively) and

their 95% confidence interval. The variables selected in the final model included confounding variables that changed the crude, unstratified odds ratio by more than 10%. The software Excel 2016 (Microsoft Corp, Redmond WA) and STATA 14 (Stata Corp 2021, College Station, TX) were used for the analysis.

Ethical consideration

The internal review boards of the Pontifical Catholic University of Chile and SSMSO reviewed and approved our study protocol which provided safeguards to guarantee the confidentiality and protection of other patients' rights.

Results

In our study cohort population, comprised 19,546 mothers, 28.8% were obese at the beginning of pregnancy. Obese women were on average 1.9 years older than those non-obese (*P-value* <0.0001), and obese were particularly over-represented in the 35+ years group (*P-value* <0.0001). Although obese women were more likely to have a mid-educational level than non-obese women, they were of lower socioeconomic level. Obese women had more often 2-3 previous pregnancies than non-obese women, and to have chronic diseases including diabetes mellitus, hypothyroidism, dyslipidemia, and hypertension than non-obese women (Table 1).

Table 1. Characteristics of mothers in the SSMSO pregnancy cohort, Chile, 2014-2018.

Characteristics	Obese n (%) / n $\bar{x}$ (SD)	Non obese n (%) / n $\bar{x}$ (SD)	Total n (%) / n $\bar{x}$ (SD)	*P*-value
n(%)	5,634 (28.8)	13,912 (71.2)	19,546 (100)	
Sociodemographic (n=19,546)				
Age in years	28.8 (5.9)	26.9 (6.1)	27.4 (6.1)	<0.0001
Age group in years				
<20	252 (4.5)	1,506 (10.8)	1,758 (9.0)	<0.0001
20-34	4,327 (76.8)	10,600 (76.2)	14,927 (76.4)	
≥ 35	1,055 (18.7)	1,806 (13.0)	2,861 (14.6)	
Marital status (n=19,546)				
Live alone	2,986 (53.0)	7,301 (52.5)	10,287 (52.6)	0.510
Live accompanied	2,648 (47.0)	6,611(47.5)	9,259 (47.4)	
Educational level (n=19,520)				
Low	873 (15.5)	1,795 (12.9)	2,668 (13.7)	<0.0001
Medium	3,855 (68.5)	9,188 (66.1)	13,043 (66.8)	
High	901 (16.0)	2,908 (20.9)	3,809 (19.5)	
Socioeconomic level (n=19,495)				
Low	3,678 (65.4)	8,302 (59.8)	11,980 (61.5)	<0.0001

Medium	1,014 (18.0)	2,502 (18.1)	3,522 (18.1)	
High	930 (16.5)	3,063 (22.1)	3,993 (20.5)	
Obstetric history				
Gestation (n=19,539)				
Primigest (1)	1,155 (20.5)	4,440 (31.9)	5,595 (28.6)	
Paucigest (2-3)	3,653 (64.9)	8,107 (58.3)	1,1760 (60.2)	<0.0001
Multigest (4+)	825 (14.7)	1,359 (9.8)	2,184 (11.2)	
Parity (n=19,543)				
Primiparous (1)	1,160 (20.6)	4,451 (32.0)	5,611 (28.7)	
Pauciparous (2-3)	3,654 (64.9)	8,113 (58.3)	1,1767 (60.2)	<0.0001
Multiparous (4+)	820 (14.6)	1,345 (9.7)	2,161 (11.1)	
Morbidity (n=19,546)				
Diabetes mellitus	795 (14.1)	1,020 (7.3)	1,815 (9.3)	
Hypothyroidism	584 (10.4)	971 (7.0)	1,555 (8.0)	<0.0001
Dyslipidemia	795 (14.1)	590 (4.2)	1,090 (5.3)	
HBP	406 (7.2)	302 (2.2)	708 (3.6)	
Drug addiction	57 (1.0)	166 (1.2)	223 (1.1)	0.272

n: number of observations; %: percentage or relative frequency. $\bar{x}$: mean; SD: standard deviation; Educational level: according to the classification of educational level in Chile; Socioeconomic level: according to the Chilean Classification of Occupations (CIUO 08.CL); HBP: High Blood Pressure.

As shown in table 2, singleton newborns in the cohort study were were more likely to be males (51.3%) (binomial proportion with p=0.5, *P*-value = 0.0003). The average gestational age was 38.4 (SD = 2.0) weeks, with 6.2% delivered before the 37 weeks of gestation; 0.4 ‰ delivered >42 weeks (i.e., post-term) and 23.1% had dystocia. The mean birthweight was 3,327.9 (SD = 575.6) grams, 6.6% were of low birthweight (<2,500 grams) and 9.2% were macrosomic (>4,000 grams). Neonatal sepsis, neonatal admission to emergency, and hospital admission occurred in 1.5 ‰, 8.82%, and 10.2%, respectively. The mean hospital stay was 8.3 (SD=7.8) days with a hospital stay greater than 7 days in most cases (97.7%). Hematological and hemorrhagic diseases during perinatal period (35.4%), respiratory and cardiac diseases during perinatal period (18.9%), and disorders related to pregnancy (13.7%) were the most frequent discharge diagnoses of the 2,062 admissions to the neonatal care units.

Table 2. Characteristics of singleton newborns in the SSMSO pregnancy cohort, Chile, 2014-2018.

Characteristics	n (%)	$\bar{x}$ (SD)
Sex (n=19,545)		
Male	10,026 (51.3)	
Female	9,519 (48.7)	
Gestational age in weeks (n=19,538)		**38.4 (2.0)**
Birth weight in grams (n=19,538)		**3,327.9 (575.6)**
Type of delivery (n= 2,117)		
Normal	1,627 (77.0)	
Dystocia	488 (23.1)	
Neonatal morbidity		
Preterm birth (n=19,546)	1,217 (6.2)	
Post-term birth (n=19,546)*	8 (0.4)	
Low birth weight (n=19,546)	1,297 (6.6)	
Fetal macrosomia (n=19,546)	1,804 (9.2)	
Neonatal sepsis (19,546) *	29 (1.5)	
Admission to emergency (19,546)	1,723 (8.8)	
Hospitalization (19,546)	2,062 (11.5)	
Hospital stay (n=2,092)		5.7 (6.1)
Hospital stay >7 days (n=2,062)	2,015 (97.7)	
Discharge diagnosis (n=2,062)		
P50-P61	730 (35.4)	
P20-P29	389 (18.9)	
P05-P08	283 (13.7)	
P90-P96	221 (10.7)	
P70-P74	144 (7.0)	
P35-P40	135 (6.6)	
P00-P04; P10-P15; P75-P80; P80-P83; Q00-Q99	160 (7.8)	
Neonatal mortality (n=19,546)	102 (5.2*)	

n: observation number or absolute frequency; %: percentage or relative frequency, $\bar{x}$: mean; SD: standard deviation. ICD-10 codes; *: per 1,000. P50-P61: hematological and hemorrhagic diseases of the perinatal period; P20-P29: respiratory and cardiac diseases of the neonatal period; P05-P08: disorders related to pregnancy; P90-P96: Disease of fetus and newborn; P70-P74: transitory endocrine diseases of fetus and newborn. P35-P40: infectious diseases of the perinatal period; P00-P04: condition of perinatal origin; P10-P15: trauma during delivery; P75-P80: digestive system disease of the fetus and newborn; P80-P83: skin disease and temperature regulation; Q00-Q99: congenital malformations, deformations, and chromosomal abnormalities.

Table 3 shows a higher occurrence of dystocia delivery, fetal macrosomia, hospital admission, and neonatal mortality among newborns of obese women compared to the non-exposed. However, both groups had similar incidences of preterm birth, post-term birth, low birth weight, neonatal sepsis, hospital stay longer than 7 days, and average days of hospital stay.

Table 3. Neonatal morbidity and mortality according to obesity at the beginning of pregnancy in the SSMSO pregnancy cohort, Chile, 2014-2018.

Neonatal morbidity and mortality	Obesity at the beginning of pregnancy [n (%)]			
	Yes [5,634]	**No** [13,912]	**RR /$\bar{x}$ diff.**	***P*-value**
Neonatal morbidity (n=19,546)				
Dystocia (n=2,117)	149/559 (26.7)	339/1,558 (21.8)	1.2	0.018
Preterm birth	377 (6.7)	840 (6.0)	1.1	0.087
Post-term birth*	2 (0.4)	6 (0.4))	1.0	0.811
Low birth weight	369 (6.6)	9.3 (6.7)	1.0	0.603
Fetal macrosomia	759 (13.5)	1,045 (7.5)	1.8	<0.001
Neonatal sepsis*	6 (1.1)	23 (1.7)	0.7	0.333
Admission to emergency	502 (8.9)	1,221 (8.8)	1.0	0.765
Hospitalization	649 (11.5)	1,413 (10.2)	1.1	0.005
Hospital stay in days [n (μ±DS)]	31 (9.3 ± 1.7)	50 (7.8 ± 9.2)	$\bar{x}$ diff.: 1.4	0.454
Hospital stay >7 days	631 (97.2)	1,384 (98.0)	1.0	0.308
Neonatal mortality (n=19,546)	39* (6.9)	63* (4.5)	1.5	0.036

n: observation number or absolute frequency; Relative Risk; $\bar{x}$ diff. = mean difference. *: rate per 1,000.

Table 4 indicates that the occurrence of preterm birth and low birth weight were higher in newborns non-exposed to excessive gestational weight gain (EGWG) compared to those exposed, while incidences of macrosomia and neonatal admission to emergency were higher in the exposed newborns to EGWG compared to those non exposed. However, the occurrence of neonatal mortality, dystocia, post-term birth, neonatal sepsis, and hospital admission were similar among exposed and non- exposed newborns to EGWG.

Table 4. Neonatal morbidity and mortality according to excessive gestational weight gain, in the SSMSO pregnancy cohort, Chile, 2014-2018.

Neonatal morbidity and mortality	Excessive Gestational Weight Gain [n (%)]			
	Yes [2,789]	**No** [11,472]	**RR /$\bar{x}$ diff.**	**P-value**
Neonatal morbidity (n=19,546)				
Dystocia (1,590)	63/264 (23.9)	304/1,326 (22.9)	1.0	0.741
Preterm birth	117 (4.2)	734 (6.4)	0.7	<0.0001
Post-term birth*	0 (0.0)	6 (0.5)	0 (0.0)	0.227
Low birth weight	123 (4.4)	792 (6.9)	0.6	<0.0001
Fetal macrosomía	379 (13.6)	980 (8.5)	1.6	<0.0001
Neonatal sepsis*	3 (1.1)	21 (1.8)	0.9	0.383
Admission to emergency	297 (10.7)	1,056 (9.2)	1.2	0.020
Hospitalization	305 (10.9)	1,287 (11.2)	1.0	0.671
Hospitalization stay in day [n (μ±DS)]	-	-	-	-
Hospitalization >7 days	-	-	-	-
Neonatal mortality (19,546)*	10 (3.6)	60 (5.2)	0.7	0.265

n: observation number or absolute frequency; RR = Relative Risk; $\bar{x}$ **diff. = mean** difference; *: rate per 1,000.

As presented in the table 5, panel A below, we observed that the risks of neonatal mortality (OR = 1.5; 95% CI = 1.1-2.3), fetal macrosomia (OR = 1.9; 95% CI = 1.7-2.1), dystocia (OR = 1.3; 95% CI = 1.1-1.6) and hospitalization (OR = 1.2; 95% CI = 1.1-1.3) were statistically significant higher among newborns of obese women compared to those non- exposed. When adjusted for maternal age, parity, maternal educational level, maternal socioeconomic level, previous maternal chronic morbidity (diabetes mellitus, high blood pressure, hypothyroidism, drug addiction), the risk of neonatal mortality (ORa = 1.5; 95% CI = 1.1-2.3) and fetal macrosomia (ORa = 1.7; 95% CI = 1.6-1.9) remained statistically significant higher, while it became borderline statistically significant for dystocia (ORa = 1.2; 95% CI = 0.9-1.6) and hospitalization (ORa = 1.1; 95% CI = 0.9-1.2).

As shown on the panel B of table 5, the risk of low birth weight (OR = 0.6; 95% CI = 0.5-0.8) and preterm birth (OR = 0.6; 95% CI = 0.5-0.8) was not elevated and seemed decreased even at a statistically significant level among newborns exposed to EGWG compared with those unexposed. However, risk of fetal macrosomia (OR = 1.7; 95% CI = 1.5-1.9) and neonatal admission to emergency (OR = 1.2; 95% CI = 1.1-1.4) was higher in newborns exposed to EGWG compared to those unexposed.

When adjusted for maternal age, parity, maternal educational level, maternal socioeconomic level, and previous maternal chronic morbidity (diabetes mellitus, high blood pressure, hypothyroidism, drug addiction), the occurrence of low birthweight (ORa = 0.6; 95% CI = 0.5-0.8) as well as for preterm birth (ORa = 0.7; 95% CI = 0.5-0.8) remained significantly decreased while elevated for fetal macrosomia (ORa = 1.8, 95 % CI = 1.6-2.0) and admission to emergency neonatal (ORa = 1.2; 95% CI = 1.1-1.4) among those exposed to EGWG compared to the unexposed.

Table 5. Obesity at the beginning of Pregnancy (OBP) and Excessive Gestational Weight Gain (EGWG) as risk of neonatal morbidity, SSMSO, Chile 2014-2018.

	Panel A							
	Obesity at the beginning of Pregnancy as risk of neonatal morbidity							
OBP	**Neonatal mortality [IC95%]**		**Fetal macrosomía [IC95%]**		**Dystocia [IC95%]**		**Hospitalization [IC95%]**	
	OR	Ora	OR	ORa	OR	ORa	OR	ORa
No	*Referent*							
Yes	1.5 [1.1-2.3]	1.5 [1.1-2.3]	1.9 [1.7-2.1]	1.7 [1.6-1.9]	1.3 [1.1-1.6]	1.2 [0.9-1.6]	1.2 [1.1-1.3]	1.1 [0.9-1.2]
	Panel B							
	Excessive Gestational Weight Gain as risk of neonatal morbidity							
EGWG	**Low birth weight [IC95%]**		**Preterm birth [IC95%]**		**Fetal macrosomia [IC95%]**		**Admission to emergency [IC95%]**	
	OR	Ora	OR	ORa	OR	ORa	OR	ORa
No	*Referent*							
Yes	0.6 [0.5-0.8]	0.6 [0.5-0.8]	0.6 [0.5-0.8]	0.7 [0.5-0.8]	1.7 [1.5-1.9]	1.8 [1.6-2.0]	1.2 [1.1-1.4]	1.2 [1.1-1.4]

Panel A: Non-obese mother at the beginning of pregnancy as referent; 95% CI: confidence interval (95%); OR: crude Odds Ratio; ORa: Odds Ratio adjusted for maternal age, parity, maternal educational level, maternal socio-economic level, previous maternal chronic morbidity (diabetes mellitus, hypothyroidism, drug addiction). OBP: obesity at the beginning of pregnancy.

Panel B: Non-Excessive Gestational Weight Gain as referent; 95% CI: confidence interval (95%); OR: crude Odds Ratio; ORa: Odds Ratio adjusted for maternal age, parity, maternal educational level, maternal socioeconomic level, previous maternal illnesses (diabetes mellitus, hypothyroidism, drug addiction). EGWG: Excessive Gestational Weight Gain.

Discussion

The findings suggest that newborns of obese mothers at the beginning of pregnancy had a 50% increased risk of neonatal death (ORa = 1.5; 95% CI = 1.1-2.3) and 70% increased risk of fetal macrosomia (ORa = 1.7; 95% CI = 1.7-2.1) compared to newborns of non-obese mothers at the beginning of pregnancy, adjusted for maternal age, parity, maternal educational level, maternal socioeconomic level, and previous maternal chronic morbidity (diabetes mellitus, high blood pressure, hypothyroidism, drug addiction).

Most of the authors who have studied maternal obesity at the beginning of pregnancy in relation to reproductive and infantile risk did not stratify the pediatric period into its neonatal and post-neonatal components, therefore studies on neonatal period specifically are infrequent. However, our results were generally consistent with the literature regarding maternal obesity during the neonatal period separately from childhood. Thus, in a case-control study carried out in the USA, Aimin *et al*., found that risk of neonatal mortality increased 1.6 times when mothers were obese at the beginning of pregnancy (OR = 1.6; 95 % CI = 1.3-1.9) than when they were not obese [25]. Likewise, through a systemic review with meta-analysis of cohort studies, Aune *et al*., reported a positive association between neonatal mortality and pre-pregnancy maternal obesity (RR = 1.1; 95% CI = 1.1-1.2) [26].

Also, De la Calle *et al*., observed in a cross-sectional study that fetal macrosomia was more frequent in overweight pregnant women (OR = 1.5; CI = 95% 1.4-2.2) and in obese pregnant women (OR = 1.9; 95% CI = 1.3-2.8) compared to those of normal weight [27]. Similarly, the results of a systematic review and meta-analysis conducted by Gaudet *et al.* showed that maternal obesity at the beginning of pregnancy [28] is positively associated with fetal macrosomia (OR = 2.2; 95% CI 1.9-2.5).

It is also observed that, for maternal BMI levels higher than normal at the beginning of pregnancy, adjusted risk of neonatal mortality and fetal macrosomia increases as the BMI level increases (Table 5). In the case of fetal macrosomia, risk is statistically significant for all levels of BMI above normal. Whereas, in case of neonatal mortality, risk is statistically significant only for BMI levels ≥ 40 kg / m^2. This suggests a possible relation exposure dose between the level of BMI at the beginning of pregnancy

with the risk of fetal macrosomia and neonatal mortality. However, the relation with BMI levels appears to be more consistent for fetal macrosomia than for neonatal mortality (annex 1 & 2).

In addition to neonatal mortality and fetal macrosomia, results evoke a higher risk of dystocia (OR = 1.3; 95% CI = 1.1-1.6) and of hospitalization (OR = 1.2; 95% CI = 1.1-1.3) for newborns of obese mothers at the beginning of pregnancy than those of non-obese mothers. However, after adjusting for confounding variables, risk becomes non-significant for both dystocia (ORa = 1.2; 95% CI = 0.9-1.6) and hospitalization (ORa = 1.1; 95% CI = 0.9-1.2).

The loss of statistical significance of the association between dystocia and maternal obesity after adjustment could be explained by the large number of missing data related to this variable in the database. In fact, valid observations corresponding to the report of type of delivery represent only (10.8%) of data analyzed. Different authors observed positive and statistically significant association between maternal obesity at beginning of pregnancy and type of delivery. Nkokia *et al*., observed maternal overweight (ORa = 1.4; 95% CI = 1.0-1.8) and maternal obesity at beginning of pregnancy (ORa = 2.1; 95% CI = 1.1-4.1) are risk factors for caesarean sections in Malawi [29]. Along the same lines, De la Calle *et al*., verified that instrumental deliveries were higher in pregnant women with overweight (OR = 1.5; 95% CI = 1.3-1.9) and obesity (OR = 1.8; 95% CI 1.5-2.2) compared to women of normal weight. In addition, the risk of cesarean section in overweight pregnant women was practically double (OR = 1.9; 95% CI 1.4-2.5) than normal weight women. Obese women suffered three times as many cesarean sections (OR = 3.1; 95% CI = 2.8-4.3) than normal weight women [27].

The relation between maternal obesity at beginning of pregnancy and neonatal hospitalization has been poorly or unclearly reported in the literature. However, our results are similar to those found by Vinturache *et al*., in a retrospective cohort study where they concluded that overweight or obesity do not independently increase the risks of neonatal admission to intensive care (ORa = 1, 4; 95 CI = 0.7–2.6) or postnatal hospital stay (ORa = 5.5; 0.4–61.7) [30].

Regarding our findings on the risk of EGWG, did not show statistically significant association with neonatal mortality (*P*-value = 0.265). On the other hand, our findings also suggest that newborns of mothers with EGWG had 1.8 (ORa = 1.8; 95% CI = 1.6-2.0) times the risk of fetal macrosomia and 1.2 (ORa = 1.2; 95% CI = 1.1-1.4) times the risk of neonatal admission to emergency of newborns of the unexposed adjusted for maternal age, parity, maternal educational level, maternal socioeconomic level, previous maternal chronic disease (diabetes mellitus, high blood pressure, hypothyroidism, drug addiction). In contrast, newborns of mothers with EGWG have a lower risk of low birth weight (ORa =

0.6; 95% CI = 0.5-0.8) and of preterm birth (ORa = 0.7; 95% CI = 0.5-0.8) with respect to mothers without EGWG, adjusted for confounding variables.

These results are consistent with some of available scientific evidence. In a retrospective cohort study, Chen and Chauhan found no statistically significant association between EGWG and neonatal mortality (OR = 1.3; 95% CI = 0.8-2.2) [31]. On the other hand, Yang *et al.*, demonstrated in China that EGWG is significantly positive associated with macrosomia (OR = 1.1; 95% CI = 1.0-1.2; *P* = 0.013) and significantly negative with low birth weight (OR = 0.9; 95% CI = 0.8-1.0; *P* = 0.045) and preterm birth (OR = 0.8; 95% CI = 0.6-0.9; *P* = 0.003) [32]. Likewise, the results of a review performed by Goldstein *et al*., showed that EGWG reduces risk of low birth weight (OR = 0.7; 95 CI = 0.6-0.7) and preterm birth (OR = 0.8; 95% CI = 0.7-0.9) [33].

Regarding admission to emergency, its relation with EGWG is not sufficiently described in the literature, so it is also poorly detailed or unclear as hospitalization. However, our findings are close to those reported in Spain by Carmona-Ruiz *et al*., where they observed that EGWG is significantly positively associated with admission to intensive care units [34].

How is it biologically plausible that maternal obesity increases risk of neonatal morbidity and mortality? One may think of one possible mechanism: maternal adipokines, including interleukin 6 (IL-6), tumor necrosis factor alpha (TNF-α), leptin, and adiponectin which are elevated in obesity in general and in maternal obesity in particular may alter the placental function. In presence of maternal obesity, hormonal dysregulation and metabolic and inflammatory changes occur that adversely affect both the placenta and the fetus, causing perinatal complications for the maternal-fetal pairing [3].

The opportunities for prevention of maternal obesity are abundant. For one, pregnancy is a critical period of life in which woman and family in general have a unique level of motivation. At the same time, there is scientific evidence that interventions to optimize maternal weight management during pregnancy based on balanced diet and controlled exercise are effective [35]. However, preventive interventions against maternal obesity should start before pregnancy so that women have a better chance of starting their pregnancy with normal weight. On the other hand, it is important to engage women of childbearing age and pregnant women at the right time to facilitate the control of gestational weight gain.

Strengths and Limitations

This study explores a research question on a problem of current global concern, using a four-year population database, in which most institutional births of the SSMSO were registered, which allows an analysis of neonatal morbidity and mortality in a large and diverse, representative study population. However, limitations of this study should be considered to properly contextualize the results. Secondary data has been used, collected for non-investigative purposes, susceptible to be imprecise and with variable recording error. One such source of errors is the variability of the quality of data collection, inherent to clinical practice, differences of staffing and training which results in incompleteness and inaccuracies of recordkeeping as shown by the variations of missingness on data of the covariates (Tables 1 & 2), and lack of standardization of birthweight, maternal height, and weight. The absence of important variables such as: APGAR score, trauma, neonatal asphyxia, intergenesic period, should be noted. Additional possible confounding variables such as smoking, alcohol and coffee consumption, previous maternal health insurance as well as the number of prenatal visits have not been recorded either. Some observations have been lost due to the presence of missing or inconsistent data. Most of the 109,879 records available in this facility during the study period, lacked complete data on the variables of interest. Although this fact may raise concerns about potential selection bias, we consider this bias rather unlikely to be present.

Conclusions

Maternal obesity at the beginning of pregnancy may be positively associated with neonatal mortality and fetal macrosomia. The risk of neonatal mortality and fetal macrosomia is directly proportional to the level of preconception maternal BMI, starting from a BMI higher than normal. EGWG is usually positively associated with macrosomia and neonatal admission to emergency, whereas it appears to be negatively associated with low birth weight and preterm birth. No association between EGWG and neonatal mortality has been demonstrated. Weight management guidelines for women of childbearing age should consider these findings to reduce the burden of fetal, neonatal, and infant morbidity and mortality. It is recommended to promote maintenance of normal weight before pregnancy and adequate gestational weight gain.

Acknowledgements

The authors would like to thank Angélica Domínguez, Mario Soto, Kelly Nuñez, Jaime Cerda, Francisco Suárez, Camilo Jaramillo Agüero, María José Fernández, Lesly Liverdieu Andrecy, Joane Adrien, Gary Sánchez, and Samson Marseille for their assistance in conducting the study.

References

1. González-Javier FP, Jiménez-Sastré A, Quevedo-Tejero EC, Guzmán-León R. Correlación de sobrepeso y obesidad con la presión arterial en adultos mayores en una unidad de primer nivel en Tabasco. *Horizonte Sanitario* 2015; 14 (1) 7-13. https://www.redalyc.org/articulo.oa?id=457844964002 Visited on July 2, 2019.

2. Nigro E, Scudiero O, Monaco ML, et al. New insight into adiponectin role in obesity and obesity-related diseases. *Biomed Res Int*. 2014;2014:14. doi:10.1155/2014/658913

3. Howell KR, Powell TL. Effects of maternal obesity on placental function and fetal development. *Reproduction*. 2017;153(3):R97. doi:10.1530/REP-16-0495

4. Organización Mundial de la Salud. Obesidad y sobrepeso. Datos y Cifras. https://www.who.int/es/news-room/fact-sheets/detail/obesity-and-overweight. Visited on July 20, 2019.

5. Nguyen T, Lau DCW. The obesity epidemic and its impact on hypertension. *Can J Cardiol*. 2012;28(3):326-333. doi:10.1016/j.cjca.2012.01.001

6. World Health Organization. Obesity and overweight. Key facts https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Visited on June 26, 2021.

7. Mohammed MS, Sendra S, Lloret J, Bosch I. Systems and WBANs for controlling obesity. *J Healthc Eng*. 2018;2018:21. doi:10.1155/2018/1564748

8. Yáñez C. Chile, entre los 10 países con más exceso de peso del mundo. LA TERCERA. https://www.latercera.com/noticia/chile-los-10-paises-mas-exceso-peso-del-mundo/ Visited on July 26, 2019.

9. Sotillo M, Monagas E, Brito-Núñez NJ, Brito-Núñez JD, Ruiz-Rendón CM. Riesgo de Diabetes en Una Comunidad Rural Del Municipio Sotillo. Estado Monagas. Venezuela. *Rev Venez Endocrinol y Metab*. 2014;12(3):167-176. http://ve.scielo.org/scielo.php?script=sci_arttext&pid=S1690-31102014000300004 Visited March 24, 2023

10. Oficina Regional de la FAO para América Latina y el Caribe. FAO/OPS: sobrepeso afecta a casi la mitad de la población de todos los países de América Latina y el Caribe salvo por Haití | FAO. http://www.fao.org/americas/noticias/ver/es/c/463396/ Visited on July 26, 2019.

11. Barrera C, Germain A. Obesidad y Embarazo. *Rev Médica Clínica Las Condes*. 2012;23(2):154-158. http://www.clc.cl/Dev_CLC/media/Imagenes/PDF revista médica/2012/2 marzo/Dr_Barrera-8.pdf Visited on July 27, 2019.

12. Bachelet VC, Lanas F. Smoking and obesity in Chile's Third National Health Survey: light and shade. *Rev Panam Salud Pública*. 2018;42(e132):5. doi:10.26633/RPSP.2018.132

13. Araya BM, Padilla O, Garmendia ML, Atalah E, Uauy R. Obesidad en mujeres chilenas en edad fértil. *Rev Med Chil*. 2014;142(11):1440-1448. doi:10.4067/S0034-98872014001100011

14. Fontaine KR, Redden DT, Wang C, Westfall AO, Allison DB. Years of Life Lost Due to Obesity. *JAMA*. 2003;289(2):187. doi:10.1001/jama.289.2.187

15. Floody PD, Lizama AC, Hormazábal MA, Poblete AO, Navarrete FC, Mayorga DJ. Evaluation of a comprehensive program of four months of duration on the preoperative conditions of obese patients candidates for bariatric surgery. *Nutr Hosp*. 2015;32(3):1022-1027. doi:10.3305/nh.2015.32.3.9350

16. Sean Meehan, Charles R. Beck, John Mair-Jenkins, Jo Leonardi-Bee RP. Maternal Obesity and Infant Mortality: A Meta-Analysis. 2014;133(5):863-871. doi:10.1542/peds.2013-1480

17. Heslehurst N, Russell S, Brandon H, Johnston C, Summerbell C, Rankin J. Women's perspectives are required to inform the development of maternal obesity services: a qualitative study of obese pregnant women's experiences. *Health Expect*. 2015;18(5):969-981. doi:10.1111/hex.12070

18. Segovia SA, Vickers MH, Gray C, Reynolds CM. Maternal obesity, inflammation, and developmental programming. *Biomed Res Int*. 2014;2014:14. doi:10.1155/2014/418975

19. Ouchi N, Kihara S, Funahashi T, Matsuzawa Y, Walsh K. Obesity, adiponectin and vascular inflammatory disease. *Curr Opin Lipidol*. 2003;14(6):561-566.

doi:10.1097/01.mol.0000103609.38789.96

20. Sun K, Kusminski CM, Scherer PE. Adipose tissue remodeling and obesity. *J Clin Invest*. 2011;121(6):2094-2101. doi:10.1172/JCI45887

21. Polskie Towarzystwo Endokrynologiczne M, Małgorzewicz S, Łysiak-Szydłowska W, Sworczak K. The serum profile of adipokines in overweight patients with metabolic syndrome. *Endokrynol Pol J Endocrinol*. 2010;61(1):36-41. https://journals.viamedica.pl/endokrynologia_polska/article/view/25408/20232. Visited on July 28, 2019.

22. Skurk T, Alberti-Huber C, Herder C, Hauner H. Relationship between Adipocyte Size and Adipokine Expression and Secretion. *J Clin Endocrinol Metab*. 2007;92(3):1023-1033. doi:10.1210/jc.2006-1055

23. Cervantes Ramírez DL, Elena M, Acosta H, et al. Prevalencia de obesidad y ganancia de peso en mujeres embarazadas. *Resid Med Fam*. 2019;26(2):5. doi:10.22201/facmed.14058871p.2019.2.68824

24. Gramage Córdoba L, Cubells A, Bellido M. Obesidad en la edad reproductiva y embarazo. Revisión de la bibliografía. *Rev Matronas*. 2015;3(1):14. https://www.enfermeria21.com/revistas/matronas/articulo/53/obesidad-en-la-edad-reproductiva-y-embarazo-revision-de-la-bibliografia/. Visited on July 28, 2019.

25. Chen A, Feresu SA, Fernandez C, Rogan WJ. Maternal obesity and the risk of infant death in the United States. *Epidemiology*. 2009;20(1):16. doi:10.1097/EDE.0b013e3181878645

26. Aune D, Saugstad OD, Henriksen T, Tonstad S. Maternal body mass index and the risk of fetal death, stillbirth, and infant death: a systematic review and meta-analysis. *JAMA*. 2014;311(15):1536-1546. doi:10.1001/jama.2014.2269

27. De la Calle FM M, Armijo L O, Martín B E, et al. Sobrepeso y obesidad pregestacional como factor de riesgo de cesárea y complicaciones perinatales. *Rev Chil Obstet Ginecol*.

2009;74(4):233-238. doi:10.4067/S0717-75262009000400005

28. Gaudet L, Ferraro ZM, Wen SW, Walker M. Maternal obesity and occurrence of fetal macrosomia: A systematic review and meta-analysis. *Biomed Res Int*. 2014;2014(2):22. doi:10.1155/2014/640291

29. Nkoka O, Ntenda PAM, Senghore T, Bass P. Maternal overweight and obesity and the risk of caesarean birth in Malawi. *Biomed Res Int*. 2019;16(1):10. doi:10.1186/s12978-019-0700-2

30. Vinturache AE, McDonald S, Slater D, Tough S. Perinatal outcomes of maternal overweight and obesity in term infants: A population-based cohort study in Canada. *Sci Rep*. 2015;5:6. doi:10.1038/srep09334

31. Chen HY, Chauhan SP. Association between Gestational Weight Gain Adequacy and Adverse Maternal and Neonatal Outcomes. *Am J Perinatol*. 2019;36(6):615-623. doi:10.1055/s-0038-1672196

32. Yang W, Han F, Gao X, Chen Y, Ji L, Cai X. Relationship between Gestational Weight Gain and Pregnancy Complications or Delivery Outcome. *Sci Rep*. 2017;7(1):9. doi:10.1038/s41598-017-12921-3

33. Goldstein RF, Abell SK, Ranasinha S, et al. Association of gestational weight gain with maternal and infant outcomes: A systematic review and meta-analysis. *JAMA - J Am Med Assoc*. 2017;317(21):2207-2225. doi:10.1001/jama.2017.3635

34. Carmona-Ruiz IO, Saucedo de la Llata E, Moraga-Sánchez MR, Cantero-Miñano MD, Romeu-Sarrió A. Ganancia de peso y resultados perinatales. *Ginecol Obs Mex*. 2016;11:12. https://ginecologiayobstetricia.org.mx/articulo/ganancia-de-peso-durante-el-embarazo-y-resultados-perinatales-estudio-en-una-poblacion-espanola-e-influencia-de-las-tecnicas-de-reproduccion-asistida Visited on March 24, 2019.

35. Farías M. Obesidad materna: severo problema de salud pública en Chile. *Rev Chil Obstet Ginecol*. 2013;78(6):409-412.

doi:10.4067/S0717-75262013000600001

ANNEXS

Annex 1

Table 2d. Risk of fetal macrosomia and neonatal mortality according to BMI at the beginning of pregnancy, SSMSO, Chile, 2014-2018.

Maternal BMI at the beginning of pregnancy	Neonatal morbidity and mortality			
	Fetal macrosomia		Neonatal mortality	
	OR [IC95%]	ORa [IC95%]	OR [IC95%]	ORa [IC95%]
18.5-24.9	*IMC normal*			
25-29.9	1.8 [1.5-2.0]	1.6 [1.4-1.9]	1.1 [0.7-18]	1.2 [0.7-1.9]
30-34.9	2.3 [2.0-2.6]	2.0 [1.7-2.3]	1.3 [0.7-2.3]	1.4 [0.8-2.4]
35-39.9	3.1 [2.6-3.8]	2.7 [2.3-3.3]	1.4 [0.6-3.1]	1.4 [0.6-3.10]
≥ 40	4.1 [3.2-5.3]	3.3 [2.6-4.3]	5.0 [2.5-10.4]	5.1 [2.4-10.7]
	X^2 trend P-value = 0.02		*X^2 trend P-value < 0.001*	

ORa: Odds Ratio adjusted for maternal age, parity, maternal educational level, maternal socio-economic level, previous maternal chronic morbidity (diabetes mellitus, hypothyroidism, drug addiction). CI: 95% confidence interval; P-value <0.05; BMI: 18.5-24.9 kg / m^2: normal weight, reference level; BMI: <18.5 kg / m^2: underweight; BMI: 25-24.9 kg / m^2: overweight; IM: 30-34 kg / m^2: moderate obesity; BMI: 35-39.9 kg / m^2: severe obesity; BMI≥40 kg / m^2: morbid obesity.

Annex 2

Figure 1. Behavior of risk of fetal macrosomia and neonatal mortality, according to maternal BMI at the beginning of pregnancy SSMSO, Chile, 2014-2018.