Pre-pregnancy overweight and weight gain during pregnancy increase the risk of gestational anemia

Cantoral Alejandra*, Center for Nutrition and Health Research, National Institute of Public Health, Av. Universidad 655, Col Sta Ma Ahucatlán, 62230, Cuernavaca, Morelos, México. Phone +52 (777) 3293000 alejandra.cantoral@insp.mx

Christensen Dirk L., Department of Public Health, Section of Global Health, University of Copenhagen. Oster Farimagsgade 5, CSS building 9, 1014, Copenhagen K, Denmark. dirklc@sund.ku.dk

Solano Maritsa, Center for Nutrition and Health Research, National Institute of Public Health, Av. Universidad 655, Col Sta Ma Ahucatlán, 62230, Cuernavaca, Morelos, México. msolano@insp.mx

Lamadrid-Figueroa Héctor¹, Center for Public Health Research, National Institute of Public Health, Av. Universidad 655, Col Sta Ma Ahucatlán, 62230, Cuernavaca, Morelos, México. hlamadrid@insp.mx

Ávila Laura, Morelos Delegation, Mexican Institute of Social Security. Blvd. Benito Juarez 18, Col Centro, 62100, Cuernavaca, Morelos, México. laura.avila@imss.gob.mx

Trejo-Reyes Rebeca, Center for Nutrition and Health Research, National Institute of Public Health, Av. Universidad 655, Col Sta Ma Ahucatlán, 62230, Cuernavaca, Morelos, México. rbk_7580@hotmail.com

Omar Domínguez-Flores, Center for Nutrition and Health Research, National Institute of Public Health, Av. Universidad 655, Col Sta Ma Ahucatlán, 62230, Cuernavaca, Morelos, México. omi_d95@hotmail.es
Abstract

**Objective:** To study the double burden of overweight and anemia in Mexican women during pregnancy and if pre-pregnancy body mass index (BMI) and weight gain are associated with the development of anemia. In a sample of 98 pregnant women from an ongoing birth cohort, weight and hemoglobin at different gestational weeks, as well as pre-pregnancy BMI (self-reported) were obtained. An adjusted logistic model for longitudinal data was used to estimate the probability of presenting anemia according to pre-pregnancy overweight status (BMI $> 25$ kg/m$^2$) and weight gain, including an interaction term between these two variables.

**Results:** At the end of pregnancy the combined prevalence of overweight and anemia was 18%. The probability of developing anemia was different from zero among overweight women at the beginning of pregnancy and weight gain $> 6.5$ kg (up to 8%, $p < 0.05$); furthermore, the prevalence was higher than zero in those women with a normal pre-pregnancy BMI ($< 25$ kg/m$^2$) and a weight gain $\leq 12$ Kg (up to 9%, $p < 0.05$). In conclusion anemia increases with the combinations of low weight gain in women with a normal pre-pregnancy BMI as well as excessive weight gain in women with pre-pregnancy overweight.

Key words: pregnancy, anemia, overweight
Introduction

In Mexico, the prevalence of overweight and obesity in women of reproductive age (20-49 years) has increased dramatically (42.4%) over the last three decades [1]. Nowadays, more than 70% of women of reproductive age have a body mass index (BMI) above 25 kg/m² [2]; furthermore, around 30% of women are expected to have a BMI > 30 kg/m² when they become pregnant [3]. At the same time, anemia has declined since the 1990s but the current prevalence of anemia in women of reproductive age is still high at 22% [4]. Furthermore, overweight and anemia during pregnancy are associated with adverse health outcomes in mother and offspring [5-7].

It has been recognized that overweight may contribute to low iron status, as BMI is negatively correlated to serum iron [8], and iron deficiency is more common in overweight than normal-weight children and women [9-12]. This correlation has been documented in Mexico since 1999, when the National Nutrition Survey showed that the risk of iron deficiency in obese children and women of reproductive age was 2–4 times that of individuals with a healthy weight at similar dietary iron intakes [10].

In the case of pregnant women, some studies have shown that a high BMI previous to and during pregnancy influence iron stores negatively [13-15]; pre-pregnant obese women have lower ferritin concentrations than pre-pregnant non-obese women [13].

Other studies have examined the association between obesity and iron status in pregnant woman and their offspring [16-18]. Although deficiencies, like anemia, and conditions of excess, such as overweight, might seem opposite to one another, they share environmental conditions and behaviors and can co-occur at the household and individual level; this co-occurrence has been named the “double burden of malnutrition” [19-21]. A previous study documented that Mexican women of reproductive age from mildly and moderately food insecure households, were more likely to experience concurrent anemia and overweight than were women from food secure households [22]. This probably reflects simultaneous overconsumption of high-energy products and nutrient-poor diets [22].
The two conditions, iron deficiency-anemia and overweight could be interlinked through: poor dietary quality, diets restricted in total iron or animal-source iron and calorie rich diets; increased iron requirements during pregnancy, or impaired iron absorption related to higher levels of hepcidin resulting from obesity-related inflammation [8, 14, 23-25].

It is highly relevant to study not only the prevalence of overweight plus anemia during pregnancy in a country where both conditions are public health problems, but also to study if the pre-pregnancy BMI and weight gain during pregnancy are associated with the development of anemia.

Main text

Methods

The study is based on a subsample of 98 pregnant women from an ongoing birth cohort study (named MAS-Lactancia, in Spanish) that was initiated in 2016, and in which over 954 pregnant women have been recruited. Mothers were considered for inclusion in the study if they were between 18 to 39 years of age, in gestation weeks between 3 to 22, planned to live in the area of Cuernavaca for 3 years after delivery, and with the intention of delivery at the IMSS General Hospital in Cuernavaca. Exclusion criteria included woman with (1) more than one fetus, (2) high-risk pregnancy, (3) history or diagnosis of hypertension, (4) hypertensive diseases of pregnancy, (5) with renal, liver, heart or cardiovascular disease, (6) endocrine disorders, (7) preterm births (<37 weeks gestation), and (8) abuse of drugs.

After reviewing the clinical files of the total sample (n=954), we included 98 pregnant women as they were the ones with complete and available information on hemoglobin and anthropometry through pregnancy. We reviewed the clinical files of participants in the study and recorded the following variables: pre-pregnancy weight (self-reported), age, and parity. During prenatal care visits weight and height were measured (Weight, using light clothing with a Bame scale, with a precision of 100 g. Height, using a Health-o-Meter stadiometer with a precision of 0.1 cm) as well as gestational age (weeks) determined by last menstrual
date or by ultrasonography. Hemoglobin levels were also obtained from the files (analyzed by UniCel DxC 600/800 SYNCHRON) and recorded in the files with the corresponding gestational age.

Pre-pregnancy BMI was estimated as weight (kg)/ height (m$^2$), and pre-pregnancy overweight was defined as $\geq25kg/m^2$. Weight gain was estimated using the pre-pregnancy self-reported weight and the current weight of each visit (by the corresponding gestational age). Anemia was defined according to WHO as adjusted hemoglobin by altitude <11.0g/dL [26].

Statistical analysis: Descriptive statistics are presented for variables at baseline as mean (SD) and ranges. A random-effects logistic regression model for longitudinal data was fit to estimate the probability of having anemia according to pre-pregnancy overweight status and weight gain, including an interaction term between these two variables. The model was adjusted for age, previous pregnancies and gestational age. All analyses were run in Stata 15.0 (StataCorp LLC)

Results

Women were followed during pregnancy, with a variation of 1 to 5 prenatal visits in the prenatal care of IMSS clinics (average 2 prenatal visits). Mean age was 28.0 (SD 4.6) years, with ~50% being overweight at the beginning of pregnancy (Table 1). We compared the analytical sample versus the rest of the cohort, and did not find any differences in the following variables: age, socioeconomic status, education level and parity (data not shown).

Mean hemoglobin was 13.0 (SD 0.0) mg/dL during recruitment and none presented with anemia. At the end of pregnancy, the median weight had increased by 9kg (IQR 6.5 – 12.0), 71% presented with overweight (BMI$\geq25$kg/m$^2$), and 18% had a combination of overweight and anemia (BMI$\geq25$kg/m$^2$ and hemoglobin <11.0g/dL); 3% presented with anemia and normal BMI (BMI< 25kg/m$^2$ and hemoglobin <11.0g/dL), and 8% had normal BMI as well as normal hemoglobin levels at the end of pregnancy.
Figure 1 presents the predicted probabilities of anemia (95% CI) of the adjusted random-effect model, which show an interaction between pre-pregnancy BMI status and weight gain (p<0.07). For those women who started the pregnancy with a normal BMI (<25kg/m²) and during pregnancy gained, 6.5kg (25th percentile), 9kg (50th percentile), and 12kg (75th percentile) the probability of presenting with anemia was 9%, 7% and 5% respectively. In contrast, for those women who started the pregnancy with overweight (BMI≥25kg/m²) and during pregnancy gained 6.5kg (25th percentile), 9kg (50th percentile) or 12kg (75th percentile) the probability of presenting with anemia was 6%, 7% and 8%, respectively. These results were adjusted for maternal age, previous pregnancies, and gestational age.

We found that the probability of presenting anemia during pregnancy increases with the combination of pre-pregnancy BMI classification and the gestational weight gain. For those with the combination of having overweight (BMI≥25Kg/m²) at the beginning of pregnancy and gestational weight gain between 6.5 to 12 kg, this probability increases up to 8%. This result is highly important for health systems, frequently facing more overweight pregnant women.

Discussion

In this sub-sample of “healthy” pregnant women, almost 50% of the participants started pregnancy with a BMI ≥25kg/m² (only one participant presented with a BMI<18kg/m² when becoming pregnant), and more than 80% finished the pregnancy with this condition (71% with overweight and 18% with overweight and anemia). Only 11% of the participants ended the pregnancy with a BMI<25 kg/m² (8% with a normal BMI and 3% with normal BMI and anemia). We observed that for women with a pre-pregnancy BMI <25 Kg/m², the probability of presenting anemia is up to 9% with a gestational weight gain lower or equal to 12kg.

Epidemiological studies have shown contradictory results regarding the association between overweight/obesity and anemia in pregnancy. Some have documented that overweight women had an increased risk of low iron status and higher levels of hepcidin and maternal
inflammation [17, 27]. Others have shown no relation of obesity during pregnancy and iron status [28]. Furthermore, a study of two cohorts showed that higher BMI in early pregnancy was positively associated with hemoglobin and reduced risk of anemia [29].

The prevalence of the double burden of overweight and anemia during pregnancy in the current study was 18%, which is a higher prevalence rate than other countries with low prevalence of overweight, like Vietnam, in which it was reported that only 2% of pregnant women presented with both conditions [30]. Our results reflect a country with a nutrition transition that is facing the double burden of malnutrition (excess and deficiency), i.e. overweight and anemia in the same individual. This could be viewed in the context of the data reported by the National Health and Nutrition Survey (2012) showing a prevalence of overweight in women (of reproductive age) above 70% and a prevalence of iron deficiency of 29% [31]. Furthermore, the survey reported a combined prevalence of overweight and anemia in women of reproductive age of 10%[22], and suggest that diet was higher in energy dense foods and inadequate in iron intake due to low availability [32]. Besides diet, iron absorption could be reduced due to higher levels of hepcidin as a result of chronic inflammation [25]. Finally, the normal hemodilution of pregnancy contributes to a decrease in hemoglobin levels; however, we tried to control for this condition by using gestational age as a covariate in the models.

Finally, our data support that pregnant women should follow the US Institute of Medicine (IOM) guidelines for healthy weight gain during pregnancy. These guidelines consider preconception BMI and suggest a range of recommended weight gain by trimester of pregnancy [33], since numerous studies have supported the suitability of these guidelines for positive pregnancy outcomes [34].

**Limitations**

- A limitation of the study was that, we consider anemia as being due to iron deficiency instead of measuring ferritin or iron stores, but it has been documented that >50% of anemia in pregnancy is due to iron deficiency [35].
• In spite of the small sample size, we estimated a statistically significant interaction, which means that with a bigger sample our findings would probably be stronger.
• The main strengths of the study is the longitudinal design with repeated measures of BMI and hemoglobin, which allowed us to capture the effect modification of pre-pregnancy overweight with the variation of gestational weight gain on the hemoglobin levels.

**Abbreviations**
BMI: Body Mass Index; IMSS: Instituto Mexican del Seguro Social; WHO: World Health Organization; SD: Standard Deviation

**Ethics approval and consent to participate**
Written informed consent was obtained from all the pregnant women include in this analysis as part of the consent of the main cohort. A copy of the written consent is available for review by the Editor-in-Chief of this journal. The study has been carried out by the National Institute of Public Health, in collaboration with the Mexican Institute for Social Security in Cuernavaca, Morelos (IMSS), ethical and research commissions approved the protocol of the cohort.

**Consent to publish**
Not applicable

**Availability of data and materials**
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests**
The authors declare that they have no competing interests.

**Funding**
National Council of Science and Technology (CONACYT grant # 233439)


Authors’ contributions

AC, MS, RT-R, OD-F: Collected the patient’s data. LA, IR-S coordinated and supervised the fieldwork. AC, DLC, HL-F drafted the manuscript. AC, HL-F made the statistical analysis. JAR, IR-S, DLC revised this manuscript critically. All authors read and approved the final manuscript.

Acknowledgements

We thank the Instituto Mexicano del Seguro Social (Cuernavaca, Morelos) for their support with this research.
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