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Original/*Otros*

Predictors of hyperlipidemia during the first half of pregnancy in Mexican women

Adriana Garduño-Alanís[1], Gilberto Vázquez-de Anda[2], Roxana Valdés-Ramos[3], Juan O. Talavera[4], Javier E. Herrera-Villalobos[1], Gerardo G. Huitrón-Bravo[2] and Eduardo Hernández-Garduño[1]

[1]Unidad de Investigación, Hospital Materno Perinatal "Mónica Pretelini Sáenz", Instituto de Salud del Estado de México (ISEM). Estado de México. México. [2]Facultad de Medicina, Universidad Autónoma del Estado de México (UAEMex). Estado de México. México. [3]Centro de Investigación y Estudios Avanzados en Ciencias de la Salud. Facultad de Medicina, Universidad Autonoma del Estado de Mexico. Estado de Mexico. Mexico. [4]Centro de Investigación en Ciencias Médicas de la Universidad Autónoma del Estado de México (UAEMex). Estado de México. México.

Abstract

Objective: To determine the predictors of hypercholesterolemia and of hypertriglyceridemia during the first half of pregnancy in Mexican women.

Methods: Cross-sectional comparative study of pregnant women with less than 21 weeks of gestational age. Measurements: Demographic information, obstetric history, prepregnancy body mass index, cholesterol and triglycerides. Cross tabulations and multiple logistic regression were used for statistical analysis.

Results: 230 participants; 61 women with normal prepregnancy body mass index, 108 with overweight, and 61 with obesity. Dyslipidemia was defined as elevated cholesterol (>180 mg/dL) or triglycerides (>170 mg/dL). After adjusting by potential confounders, independent predictors of hypercholesterolemia included being overweight (OR=2.8, 95% CI 1.4-5.9), being obese (OR=3.7 95% CI 1.6-8.4) or being on the second trimester of pregnancy. The same predictors were found for hypertriglyceridemia, respectively OR=2.8, 95% CI 1.4-5.6, OR=2.9, 95% CI 1.3-6.5, OR=2.6, 95% CI 1.4-4.7.

Conclusion: Mexican women with prepregnancy overweight or obesity have greater risk of suffering hypercholesterolemia and hypertriglyceridemia during pregnancy. Women in the second trimester had higher levels of both lipids as compared to the first one. This is the first Mexican study that confirms the increase of lipids as gestational age progresses.

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Key words: *Cholesterol. Triglycerides. Pregnancy. Overweight. Obesity.*

Correspondence: Garduño-Alanís Adriana PhD.
Unidad de Investigación. Hospital Materno Perinatal
"Mónica Pretelini Sáenz" Paseo Tollocan s/n, Col. Universidad,
C.P.50130. Toluca, Estado de México, México.
E-mail: adrisgamx@hotmail.com

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PREDICTORES DE HIPERLIPIDEMIA DURANTE LA PRIMERA MITAD DEL EMBARAZO EN MUJERES MEXICANAS

Resumen

Objetivo: Determinar los predictores de hipercolesterolemia y de hipertrigliceridemia durante la primera mitad del embarazo en mujeres Mexicanas.

Métodos: Estudio transversal comparativo de mujeres embarazadas con menos de 21 semanas de edad gestacional. Mediciones: información demográfica, historia obstétrica, índice de masa corporal pregestacional, niveles sanguíneos de colesterol y triglicéridos. Se usaron tabulaciones cruzadas y regresión logística múltiple en el análisis estadístico.

Resultados: 230 participantes; 61 mujeres con índice de masa corporal pregestacional normal, 108 con sobrepeso, y 61 con obesidad. Dislipidemia se definió como elevación de colesterol (>180 mg/dL) ó triglicéridos (>170 mg/dL). Después de ajustar con potenciales variables de confusión, los predictores independientes de hipercolesterolemia incluyeron sobrepeso (OR=2.8, 95% CI 1.4-5.9), obesidad (OR=3.7 95% CI 1.6-8.4) o estar en el segundo trimestre del embarazo. Los mismos predictores se encontraron para hipertrigliceridemia, respectivamente: OR=2.8, 95% CI 1.4-5.6, OR=2.9, 95% CI 1.3-6.5, OR=2.6, 95% CI 1.4-4.7.

Conclusión: Mujeres Mexicanas con sobrepeso u obesidad pregestacional tienen mayor riesgo de presentar hipercolesterolemia e hipertrigliceridemia durante el embarazo. Mujeres en el segundo trimestre tuvieron niveles más altos de ambos lípidos comparando con el primer trimestre. Este es el primer estudio Mexicano que confirma el incremento de lípidos conforme la edad gestacional progresa.

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Palabras clave: *Colesterol. Triglicéridos. Embarazo. Sobrepeso. Obesidad.*

Abbreviations

LGA: Large for gestational age.
PTB: Preterm birth.
PIH: Pregnancy-induced hypertension.
PBMI: Prepregnancy body mass index.

Introduction

During normal pregnancy women show an increase in levels of cholesterol and triglycerides as gestational age progresses[1-4]. Both lipids are essential for fetal development during pregnancy but high levels of cholesterol and/or triglycerides have been associated with poor health outcomes in the mother and baby including large for gestational age (LGA)[5,6] preeclampsia[7] preterm birth (PTB)[8] and pregnancy-induced hypertension (PIH)[9]. Lipid profile studies during the first half of pregnancy have been documented[2].

A recent Dutch study of pregnant women during early gestation showed that an increase in triglycerides was linearly associated with an increased risk of PIH, preeclampsia, LGA and induced preterm delivery. Total cholesterol was not associated with any of the outcome measures[10]. Evidence has also shown that exposure of the baby to mother's dyslipidemia has been associated with cardiovascular diseases in adulthood[11-13].

It has been documented that lipids increase during the second half of pregnancy and obesity favors the increase. However the role of initial weight at the beginning of pregnancy and whether it is a promoter of a substantial increase of lipids or whether there is an independent or an additive effect between mother's weight and gestational age is not well defined. There are no previous studies analyzing levels of cholesterol and triglycerides in Mexican women in early pregnancy.

Objective

In this study we determined the predictors of high cholesterol and triglycerides in the first half of pregnancy in Mexican women.

Materials and methods

In this prospective cross-sectional study, all participants were seen from August 2009 to May 2010 at the Women's and Children tertiary care hospital "Monica Pretelini Sáenz" located in Toluca in the State of Mexico. This 180 bed-hospital services women and their children with obstetric, gynecological or pediatric disorders. Patients are referred from regional primary care clinics and hospitals under the jurisdiction of the Ministry of Health in the State of Mexico.

Pregnant women who met the inclusion criteria were invited to participate in this cross-setional study during their prenatal visits with the obstetric care provider. Inclusion criteria included age 18 to 35 years, being at less than 21 weeks gestation, having a single pregnancy and prepregnancy body mass index (PBMI) higher than 18.5. Women with chronic diseases like diabetes, hypertension, those with multiple pregnancies or women taking lipid altering medication (e.g. Statins, Niacin, Bile-acid resins, Fibric acid derivatives, sleep medication drugs, antiepileptic, antidepressants, thyroid hormones, steroids, insulin etc) were excluded. Women meeting inclusion criteria accepted to participate by signing consent. Case report forms included the following information: identification number, name, age, phone number, date of recruitment, level of education, occupation, prepregnancy weight and height and gestational age calculated from the last menstrual period. The PBMI was defined as the women's weight in kilograms divided by the square of their height in meters. Women were allocated to three groups according to their PBMI, based on the classification proposed by the Institute of Medicine (US)[14]: Group "normal weight" included 61 women with PBMI of 18.6-24.9, group "overweight" included 108 women (PBMI of 25.0-29.9) and group "obesity" included 61 women (PBMI of 30.0 or higher). A 12 hour fasting blood sample for cholesterol and triglycerides analysis was collected and gestational age was calculated at the time of entry into the study after women signed the consent form. Samples were processed at the Pretelini hospital using SIEMENS Dimension® Clinical Chemistry System. Dyslipidemia was defined as elevated cholesterol (>180 mg/dL) or triglycerides (>170 mg/dL). These concentrations were at quantile 3 or about >1 standard deviation above the mean value in the group with normal weight and were similar to the criteria used to define dyslipidemia in nonpregnant adults[15].

Predictors of hyperlipidemia were determined using the mean values of women with normal weight as the cutoff points for high cholesterol (>159.5 mg/dL) and high triglycerides (>145.5 mg/dL). The statistical analysis was done by using SPSS. Descriptive statistics, including cross-tabulations of demographic and clinical characteristics by group and by level of lipids were computed. The χ^2 test, Fisher's exact or T-test when applicable, were used in a univariable analysis to assess for any in between-groups differences. Statistical significant variables ($p \leq 0.05$) were then included in multivariable logistic regression models using the backward elimination procedure, a p-value of 0.2 was set in order for variables to be included in the final models. Cholesterol levels of >180 vs. <180 mg/dL or triglycerides >170 vs. <170 mg/dL were the dependent variables. Multivariable models were constructed separately for cholesterol and triglycerides. The study received Institutional Review Board approval.

Results

The mean age of the women (n=230) was 25.3 (SD 5.2), 79% completed at least elementary school, 90.4%

were housewives, 34.8% were in the second trimester, 39.1% were nulliparous and 73.5% were overweight or obese. The overall mean level of cholesterol was 175.5 mg/dL (SD 37.3) and of triglycerides was 167.0 mg/dL (SD 55.2). Both lipids were positively correlated with each other (r^2 0.41) and with gestational age (cholesterol vs. gestational age r^2=0.24, triglycerides vs gestational age r^2=0.24). Univariable analysis showed that compared to overweight and obese women, those with normal weight were more likely to be younger, more educated, had less parity and had lower levels of cholesterol and triglycerides (p<0.05), table I. Women in the second trimester were more likely to have higher levels of cholesterol compared to women in the first trimester (77.1% vs 22.9% respectively, p=0.001) the same trend was found for triglycerides (respectively 77.8% vs 22.2%, p=0.0005), table II. In women with normal weight, the levels of cholesterol were statistically higher in the second trimester compared to the first but those of triglycerides were similar in both periods (data not shown). There was no statistically significant difference for all other variables with regard to levels of both lipids, table II. After controlling by age, level of education, gravidity and occupation, the multivariable logistic regression analysis showed that being overweight (OR=2.8, 95% CI 1.4-5.9), being obese (OR=3.7 95% CI 1.6-8.4) or being in the second trimester of pregnancy were independently associated with hypercholesterolemia. The same predictors were found for hypertriglyceridemia (being overweight OR=2.8, 95% CI 1.4-5.6,

Table I
Characteristics of pregnant women by group

	Normal weight		*Overweight*		*Obesity*		*Total*	
	n=61	*%*	*n=108*	*%*	*n=61*	*%*	*n=230*	*%*
Age (years)								
Mean (SD)	23.1 (4.8)		25.6 (5.3)		27 (4.5)		25.3 (5.2)	
18 to 24	42*	68.9	50	46.3	21**	34.4	113	49.1
25 to 35	19	31.1	58	53.7	40	65.6	117	50.9
Level of education								
Elementary	2*	3.3	28	25.9	18**	29.5	48	20.9
at least high school	59	96.7	80	74.1	43	70.5	182	79.1
Occupation								
Housewife	53	86.9	96	88.9	59	96.7	208	90.4
other	8	13.1	12	11.1	2	3.3	22	9.6
Duration of pregnancy								
first trimester	27	44.3	34	31.5	19	31.1	80	34.8
second trimester	34	55.7	74	68.5	42	68.9	150	65.2
Gravidity								
one	35*	57.4	41***	38.0	14**	23.0	90	39.1
at least 2	26	42.6	67	62.0	47	77.0	140	60.9
Cholesterol								
mean (SD)	159.5 (30.7)*		182.8 (41.2)		178.6 (31.6)**		175.5 (37.3)	
≤180 mg/dL	46*	75.4	58	53.7	30**	49.2	134	58.3
>180 mg/dL	15	24.6	50	46.3	31	50.8	96	41.7
Triglycerides								
mean (SD)	145.5 (44.2)*		173.8 (55.4)		176.8 (59.7)**		167.0 (55.2)	
≤170 mg/dL	46	75.4	55	50.9	30**	49.2	131	57.0
>170 mg/dL	15	24.6	53	49.1	31	50.8	99	43.0

Numbers are n= and column percentage unless otherwise specified.
SD = standard deviation mg/dL = miligrams per deciliter blood.
p-value of ≤0.05 by Chi-square, Fisher's exact test or T-test between groups with normal weight and overweight*, between normal weight and obesity** and between overweight and obesity***.

Table II
Characteristics of pregnant women by level of lipids

	Chorestelrol level (mg/dL)				*p-value*	*Total*		*Triglycerides level (mg/dL)*				*p-value*	*Total*	
	≤180		*>180*					*≤180*		*>180*				
	n=134	*%*	*n=96*	*%*		*n=230*	*%*	*n=134*	*%*	*n=96*	*%*		*n=230*	*%*
Age (years)														
18 to 24	64	47.8	49	51.0	0.62	113	49.1	69	52.7	44	44.4	0.21	113	49.1
25 to 35	70	52.5	47	49.0		117	50.9	62	47.3	55	55.6		117	50.9
Level of education														
Elementary	30	22.4	18	18.8	0.50	48	20.9	22	16.8	26	26.3	0.08	48	20.9
at least high school	104	77.6	78	81.3		182	79.1	109	83.2	73	73.7		182	79.1
Occupation														
Housewife	124	92.5	84	87.5	0.20	208	90.4	116	88.5	92	92.9	0.26	208	90.4
other	10	7.5	12	12.5		22	9.6	15	11.5	7	7.1		22	9.6
Duration of pregnancy														
first trimester	58	43.3	22	22.9	0.001	80	34.8	58	44.3	22	22.2	0.001	80	34.8
second trimester	76	56.7	74	77.1		150	65.2	73	55.7	77	77.8		150	65.2
Gravidity														
One	57	42.5	33	34.4	0.21	90	39.1	57	43.5	33	33.3	0.11	90	39.1
at least 2	77	57.5	63	65.6		140	60.9	74	56.5	66	66.7		140	60.9

Numbers are n = and column percentage.

Table III
*Multivariable analysis showing associated factors of hight chorestherol and triglycerides at two different cut-offs**

	Chorestelrol >159.5				*Chorestelrol >180*				*Triglycerides >145.5*				*Triglycerides >170*			
	*OR*** *	*95% CI*		*p-value*	*OR*	*95% CI*		*p-value*	*OR*	*95% CI*		*p-value*	*OR*	*95% CI*		*p-value*
Elementary school	—	—	—	—	0.6	0.3	1.2	0.134	—	—	—	—	—	—	—	—
Housewife	0.4	0.1	1.4	0.154	0.5	0.2	1.3	0.160	—	—	—	—	—	—	—	—
Gravidity >1									1.6	0.9	2.8	0.095				
Overweight	—	—	—	—	2.8	1.4	5.9	0.005	1.6	0.9	2.9	0.091	2.8	1.4	5.6	0.005
Obesity	2.4	1.2	4.9	0.016	3.7	1.6	8.4	0.002	—	—	—	—	2.9	1.3	6.5	0.007
Second trimester	1.7	0.9	3.4	0.115	2.4	1.3	4.3	0.005	2.4	1.4	4.3	0.002	2.6	1.4	4.7	0.002

*by multiple logistic regression models using the backward elimination procedure. A p-value of 0.2 was set in order for variables to be included in the final model. After controlling by age, level of education, occupation and gravidity.
**values of cholesterol and triglycerides are in mg/dL ***OR odds ratio. CI confidence interval.

obesity OR=2.9, 95% CI 1.3-6.5 or being in the second trimester of pregnancy OR=2.6, 95% CI 1.4-4.7), table III. Interaction terms for overweight*second trimester or for obesity*second trimester were not statistically significant (P values for interaction ranged from 0.50–0.86, data not shown). Using the mean values of pregnant women with normal weight as the cut-off point for hyperlipidemia, the only predictor of hypercholesterolemia was obesity (OR=2.4, 95% CI 1.2-4.9) and for hypertriglyceridemia was being in the second trimester (OR=2.4, 95% CI 1.4-4.3).

Discussion

This first study in Mexican Hispanic women adds to the evidence in showing progressive increase in the levels of lipids during pregnancy. In this study we found that being overweight or obese were independent risk factors associated with hypercholesterolemia or hypertriglyceridemia in the first half of pregnancy. The levels of both lipids were higher during the second as compared to the first trimester of pregnancy and this effect was independent of being overweight or obese. Lowering the cut-off point to the mean levels of lipids in women with normal weight showed that the only predictor of high cholesterol was obesity and for high triglycerides was being in the second trimester. This may indicate that the progressive increase in triglycerides starts at lower levels during the second trimester as compared to cholesterol. A recent study found that increase of triglycerides (but not cholesterol) was linearly associated with an increased risk of pregnancy-induced hypertension (PIH), preeclampsia, large for gestational age (LGA) and preterm delivery[10]. In our study, overweight or obese Mexican women will have an increased risk of respectively 180% and 270% for having hypercholesterolemia as compared to women of normal weight. The risk for hypertriglyceridemia increased 180% in overweight and 190% obese women. Overweight and obesity are known risk factors for pregnancy related hypertension with respect, as well as irrespectively, to hyperlipidemia. Women in the second trimester of pregnancy had an increased risk of hypercholesterolemia of 140% and of hypertriglyceridemia of 160% as compared to those in the first trimester. A study from Malaysia also found progressive increase in lipids with higher levels of lipids in the third trimester as compared to the second trimester[16]. This confirms that levels of lipids are positively correlated with gestational age. Further research is needed to determine whether high levels of lipids in Mexican women with normal weight are associated with increased perinatal morbidity and/or mortality of mother and child and to determine whether degree of increase in lipids varies in Mexican Hispanic women as compared to other ethnic groups. The fact that the progressive increase in lipids during pregnancy is independent of PBMI underscores the importance of a low lipid diet in overweight/obese women as high levels

of cholesterol and/or triglycerides have been associated with (LGA)[5,6] preeclampsia[7] preterm birth (PTB)[8] and (PIH)[9]. Furthermore, overweight and obesity increase the risk of complications during pregnancy[17,18] including congenital malformations, preeclampsia, venous thromboembolism, fetal death, miscarriage, diabetes mellitus gestational, higher rates of caesarean delivery, longer hospitalization stay, risk of infections and the presence of fatty streaks in the fetus among others[12,19,20].Children of obese or diabetic women are at risk for developing metabolic syndrome due to the presence of dyslipidemia or hyperglycaemia in the mother with consequences to their child's development underscoring the need for adequate medical and nutritional management[20-23].

Appropriate nutrition has been shown to reduce the risk of developing pregnancy-related diseases[24].

Limitations of the study include selection bias introduced because the prepregnancy lipid levels of all women were unknown. Some women with high levels of lipids may have had high cholesterol or triglycerides before pregnancy and therefore the hyperlipidemia would not be related to pregnancy. Follow up was not possible for all women therefore the rates of mother and child morbidity-mortality among the groups is not fully known which is another limitation of our study. In conclusion, overweight or obese Mexican women are predictors of hyperlipidemia and the levels of lipids progressively increase with gestational age. Counselling on the importance of pre-pregnancy BMI control prior to pregnancy and appropriate weight control during pregnancy are important efforts that would affect the levels of lipids during pregnancy. Monitoring lipids and weight control during pregnancy with adequate diet counseling is recommended to prevent hyperlipidemia related poor outcomes in mother and child.

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