

**Alteraciones bioquímicas y celulares para preeclampsia
en mujeres embarazadas que asisten al Hospital General
Dr. Raymundo Abarca Alarcón, Guerrero, México**

***Biochemical and cellular alterations for preeclampsia in pregnant women
attending the general hospital Dr. Raymundo Abarca Alarcon, Guerrero,
Mexico***

***Alterações bioquímicas e celulares da pré-eclâmpsia em gestantes
atendidas no Hospital Geral Dr. Raymundo Abarca Alarcón, Guerrero,
México***

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Resumen

La preeclampsia (PE) es una enfermedad multisistémica y multifactorial, es una de las complicaciones médicas más comunes y peligrosas en el embarazo. En México la muerte por preeclampsia se ha incrementado de 22 % a 33 %, por lo que aún es considerada la primera causa de muerte materna. Identificar los parámetros sociodemográficos, bioquímicos y antropométricos que influyen en el embarazo y la aparición de preeclampsia en mujeres embarazadas que acuden al Hospital General Dr. Raymundo Abarca Alarcón (HGRAA) en Chilpancingo de los Bravo, Guerrero, México. Se realizó un estudio transversal descriptivo en mujeres embarazadas, monitoreadas durante el periodo julio 2016 – junio 2017. Se incluyeron pacientes embarazadas con más de 20 semanas de gestación aparentemente sanas. Se obtuvieron medidas antropométricas, medición de la tensión arterial, respuestas a las encuestas aplicadas a las pacientes y recolección de muestras para la determinación de parámetros bioquímicos y celulares.

Se encontraron niveles de colesterol que van desde 99 a 443 mg/dL y triglicéridos que oscilan desde 80 a 532 mg/dL, 3.58 % presentaron glucosa basal anormalmente alta, así como también un 28.92 % de las pacientes presentaron curvas anormales con la glucosa postprandial y 38.33 % de las pacientes presentaron un hematocrito bajo. Se detectó 1.14 % de pacientes que cumplen con los criterios diagnósticos de preeclampsia, 0.57 % como candidato a adquirir la enfermedad y 98.29 % como pacientes normales.

Palabras clave: Dislipidemias, IMC, percentil 95, preeclampsia, presión arterial.

Abstract

Preeclampsia (PE) is a multisystemic and multifactorial disease, it is one of the most common and dangerous medical complications in pregnancy. In Mexico, death from preeclampsia has increased from 22% to 33%, which is why it is still considered the first cause of maternal death. To identify sociodemographic, biochemical and anthropometric parameters that influence pregnancy and the appearance of preeclampsia in pregnant women who attend the General Hospital Dr. Raymundo Abarca Alarcón in Chilpancingo de los Bravo, Guerrero, Mexico. A descriptive cross-sectional study was carried out on pregnant women, monitored during the period July 2016 - June 2017. Pregnant patients with more than 20 apparently healthy gestation weeks were included. Anthropometric measurements, blood pressure measurements, responses to surveys applied to patients and collection of samples for the determination of biochemical and cellular parameters were obtained. Cholesterol levels ranging from 99 to 443 mg / dL and triglycerides ranging from 80 to 532 mg / dL were found, 3.58 % had abnormally high basal glucose, as well as 28.92 % of the patients presented abnormal curves with postprandial glucose and 38.33 % of the patients presented a low hematocrit. 1.14 % of patients who met the diagnostic criteria with preeclampsia were detected, 0.57 % as a candidate to acquire the disease and 98.29 % as normal patients.

Keywords: Blood pressure, BMI, dyslipidemias, 95th percentile, preeclampsia.

Resumo

A pré-eclâmpsia (PE) é uma doença multissistêmica e multifatorial, é uma das complicações médicas mais comuns e perigosas na gravidez. No México, a morte por pré-eclâmpsia aumentou de 22% para 33%, razão pela qual ainda é considerada a primeira causa de morte materna. Identificar os parâmetros sociodemográficos, antropométricos e bioquímicos que influenciam a gravidez eo início da pré-eclâmpsia em mulheres grávidas que frequentam o Hospital Geral Dr. Raymundo Abarca Alarcón (HGRAA) em Chilpancingo, Guerrero, México. Um estudo transversal foi realizado em mulheres grávidas monitoradas durante o período de julho de 2016 - junho de 2017. Os pacientes com gravidez mais de 20 semanas de gravidez, aparentemente saudáveis. Medidas antropométricas, medidas de pressão arterial, respostas a pesquisas aplicadas a pacientes e coleta de amostras para a determinação de parâmetros bioquímicos e celulares foram obtidas.

os níveis de colesterol que variam 99-443 mg / dL e triglicídos variando 80-532 mg / dL, 3,58% de glucose tinha basal anormalmente elevados foram encontrados, bem como 28,92% dos pacientes tiveram curvas anormais com pós-prandial de glucose e 38,33% dos pacientes apresentavam baixo hematócrito. 1,14 % dos pacientes que preenchem os critérios de diagnóstico de pré-eclâmpsia, foi detectado 0,57 % como um candidato a adquirir a doença e 98.29 % em pacientes normais.

Palavras-chave: Dislipidemias, IMC, percentil 95, pré-eclâmpsia, pressão arterial.

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Introduction

Preeclampsia (PE) is a multisystemic and multifactorial disease, characterized by the appearance of hypertension and proteinuria after 20 weeks of gestation (Carputo and Barranco, 2013). It is one of the most common and dangerous medical complications in pregnancy (Schmidt, Christensen & Knudsen, 2017). It affects 3 to 10% of pregnancies worldwide and is associated with significant maternal and fetal morbidity and mortality (Álvarez, Prieto and Álvarez, 2016).

In Mexico death from preeclampsia has increased from 22% to 33%, so it is still considered the first cause of maternal death (López, Manríquez, Gálvez and Ramírez, 2012). Most cases of preeclampsia occur in healthy pregnant women. Therefore, it is important to establish the risk factors that can influence the development of this pathology (Torres, 2016). Risk factors for the development of preeclampsia include chronic hypertension, diabetes, maternal age, obesity, history of preeclampsia, thrombophilias, autoimmune disorder, vascular disease (Jadli, Sharma, Damania, Satoskar, Bansal, Ghosh & Shetty, 2015).

Age becomes a risk factor for preeclampsia-eclampsia when pregnancy occurs during adolescence and advanced maternal age (Valdés and Hernández, 2014). However, also the history of preeclampsia or hypertension in previous pregnancies becomes an important element in the obstetric history of patients (Suárez, Gutiérrez, Cairo, Marín, Rodríguez and Veitia, 2014). So, 20 and 50% of pregnant women return to present this disease in their next pregnancy (Huapalla, 2017). They also increase the risk of future heart disease, stroke and increased risk of diabetes (Seely,

Tsigas & Rich, 2015). The effect of diabetes mellitus on the increased incidence of preeclampsia is probably related to a variety of factors that cause oxidative stress and endothelial damage. (Gutiérrez, 2017).

Obesity is another risk factor for the development of preeclampsia (Myers, 2017), causing an excessive expansion of blood volume and an exaggerated increase in cardiac output, which contributes to raising blood pressure (Sánchez, 2009). Likewise, women with a gestational weight gain greater than that recommended have an increased risk of hypertension associated with pregnancy (Zonana, Baldenebro and Ruiz, 2010). According to another study, obesity is attributed a major and statistically significant risk for the development of late onset of preeclampsia. (Durst, Tuuli, Shout, Macones & Cahill, 2016).

On the other hand, the physiopathological role of dyslipidemias leads to a state of oxidative stress and generation of free radicals that can contribute to endothelial dysfunction in preeclampsia (Herrera, Garay, Adaya, Camacho, Garduño and Nava, 2010). In a study conducted by Duarte, Pérez, Espinoza, Eng-Castro, Calvo, Sánchez and Romero, (2014) it was found that the concentration of triglycerides is directly related to the severity of preeclampsia. Other studies suggest that high cholesterol levels detected before or during the first trimester of pregnancy are considered predictors of the development of preeclampsia (Miguel, Salinas and Corella, 2013). However, the increase in lipids is physiological during pregnancy and is due to hormonal variations (Ywaskewycz-Benítez, Bonneau, Castillo-Rascón, López, and Pedrozo, 2010). There are no well-balanced tables or percentiles of lipids during pregnancy and their assessment is non-specific (Aguilar-Cordero, Baena-García, Sánchez-López, Guisado-Barrilao, Hermoso-Rodríguez, Mur-Billar and Capel-Tuñón, 2015). Although the work of Ywaskewycz-Benítez, et al. (2010) has to do with lipid profile values per trimester of gestation from 1 to 3, with the highest quarter of the 95th percentile of cholesterol: 230 mg / dL, 290.1 mg / dL and 321 mg / dL, respectively; while for triglycerides this 95th percentile was: 158 mg / dL, 257.4 mg / dL and 371.1 mg / dL respectively for each of the quarters in a progressive order. Although his research does not provide a reference interval for triglycerides and cholesterol during pregnancy, it is an important reference.

Other reasons that influence the development of the disease are inefficient health systems, as well as low socioeconomic, cultural and educational levels. This disease remains a latent challenge for biomedical research, as its etiology is still unknown, which complicates its prediction, its early detection, its prevention and its management or treatment. At the local level, the state of Guerrero is considered, according to the Ministry of Health, as one of the states with a high maternal mortality ratio, related to this pathology. Therefore, it was decided to carry out a study with the objective of identifying biochemical and cellular alterations for preeclampsia, through an analysis and relationship of anthropometric, biochemical and cellular measurements, in pregnant women who come to the Dr. Raymundo Abarca Alarcón General Hospital in Chilpancingo of the Braves, Guerrero.

Material and methods

A descriptive cross-sectional study was conducted in pregnant women assigned to the Dr. Raymundo Abarca Alarcón General Hospital, in Chilpancingo de los Bravo, Guerrero, Mexico, monitored during the period July 2016 - June 2017. Pregnant patients with more than 20 weeks gestation were included. , apparently healthy, with complete clinical file and with the consent to participate in the study.

The data were collected during the prenatal consultation: anthropometric measurements (weight, height and BMI), measurement of blood pressure, responses to surveys applied to patients and collection of samples for the determination of biochemical parameters (serum glucose, glucose postprandial, urea, creatinine, uric acid, cholesterol, triglycerides, TGO, TGP, albumin, direct bilirubin, total bilirubin, LDH). These samples were processed in the Cobas Integra 400 equipment (Roche diagnostics) and, for the determination of blood count (erythrocytes, hemoglobin, hematocrit, MCV, HCM, CHMC, RDW / CV, RDW / SD, platelets, VPM, differential count) were carried out in the blood count Wiener Lab Counter 19 (Wiener Lab), and processed in the Laboratory of Physiopathology and Metabolism of the Higher School of Natural Sciences.

The data was processed through the Excel 2010 program and with the statistical package Small Stata version 14.2. Measuring central tendency (mean) and dispersion measures (standard deviation) for the quantitative variables, as well as obtaining the minimum and maximum values

of each parameter, we also determined the value of p using an analysis of Anova of a factor for 3 levels.

Results

The present study was carried out in the Dr. Raymundo Abarca Alarcón General Hospital during the period from July 2016 to June 2017, in the area of gynecology and obstetrics. The patients were pregnant women who come to this nosocomial unit. Table 1 describes the percentage of general sociodemographic characteristics, such as biweekly income per family, occupation, level of study and type of housing for patients.

Tabla 1. Características sociodemográficas de las pacientes

	Datos generales	Porcentaje %
Ingresos	No contestó	2.87%
	\$80.93 USD	64.37%
	\$134.89 USD	15.52%
	\$188.85 USD	9.20%
	\$242.81 USD	2.87%
	\$269.78 USD	5.17%
Ocupación	No trabaja	0.57%
	Ama de casa	79.31%
	Profesionista	14.37%
	Comerciante	1.15%
	Estudiante	4.6%
Nivel de estudio	No contesto	2.3%
	Primaria	13.22%
	Secundaria	32.18%
	Bachillerato	28.74%
	Licenciatura	18.39%
	Maestría	1.15%
	Ninguno	4.02%
Tipo de vivienda	No contestó	2.87%
	Cemento	56.32%
	Madera	30.46%
	Adobe	5.75%
	Lamina	4.60%

Fuente: Datos de la investigación.

Table 2 shows the mean and standard deviation of each of the parameters of blood chemistry, minimum and maximum values are also observed. Alterations in patients are presented according to the reference values in several parameters, such as urea with 67.95%, creatinine with 79.55%, cholesterol with 69.61% and triglycerides with 92.26%, in relation to the reference values of a population of women not pregnant.

Tabla 2. Datos estadísticos de los parámetros bioquímicos en las pacientes embarazadas del Hospital General Dr. Raymundo Abarca Alarcón

Variable	U	Media	DS	Mín.	Máx.	% Anormales
Glucosa Sérica	mg/dL	83.665	16.631	52	218	3.58
Glucosa Postprandial	mg/dL	123.786	38.681	67	314	28.92
Urea	mg/dL	13.405	4.399	4.71	42	67.95
Creatinina	mg/dL	0.381	0.126	0.2	1.0	79.55
Ácido Úrico	mg/dL	3.925	1.033	2.09	7.69	4.41
Colesterol	mg/dL	229.555	50.336	99	443	69.61
Triglicéridos	mg/dL	247.359	83.233	80	532	92.26
TGO	u/L	18.9363	10.069	7	63	10.05
TGP	u/L	17.638	16.599	3	105	28.72
Albumina	g/dL	3.660	0.275	3.01	4.62	0
Bilirrubina Total	mg/dL	0.302	0.197	0.0	1.44	1.68
Bilirrubina Directa	mg/dL	0.128	0.120	0.03	1.1	2.24
LDH	u/L	349.963	95.021	191	669	36.66

Fuente: Datos de la investigación.

Tabla 3. Estadísticos de la citometría hemática presente en las mujeres embarazadas

Variable	u	Media	DS	Mín	Máx	% Anormales
Eritrocitos	x 10 ⁶ /uL	4.083	0.399	1.86	5.15	58.88
Hemoglobina	g /dL	12.103	1.271	5.1	15.1	60.55
Hematocrito	%	37.109	4.273	10	47.8	38.33
VCM	fL	90.686	8.110	36.4	104.1	5
HCM	pg	29.605	2.230	17.1	34.4	14.44
CHMC	g /dL	32.400	0.914	28.6	35	4.44
RDW/CV	%	14.861	0.875	11.1	18.8	6.66
RDW/SD	fL	48.897	3.214	38.7	57.7	22.77
Plaquetas	x 10 ³ /uL	224.638	59.750	22	397	8.33
VPM	fL	9.394	1.017	3.4	12.7	2.22
Leucocitos	x 10 ³ /uL	8.912	2.139	2.6	17	15.08
Segmentados	%	67.865	7.334	39	86	35.19
Basófilos	%	2.413	1.990	0	10	7.26
Eosinófilos	%	1.016	1.098	0	7	0.55
Monocitos	%	4.050	3.153	1	36	3.91
Linfocitos	%	24.525	6.352	9	42	22.90

Fuente: Datos de la investigación.

As can be seen in Table 3, the outstanding parameters that present abnormalities in blood count are erythrocytes and hemoglobin, since most of the patients present values below the reference value.

Tabla 4. Estadísticos de la relación del índice de masa corporal en contraste con las presiones arteriales en las pacientes embarazadas del HGRAA.

Variable	IMC	Media	DS	Min	Max	p
Presión arterial sistólica	Normal	111.045	12.685	95	159	0.0439
	Sobrepeso	113.526	10.143	93	136	
	Obesidad	117.150	11.523	98	154	
Presión arterial diastólica	Normal	62.772	11.342	48	106	0.0374
	Sobrepeso	66.903	7.618	51	89	
	Obesidad	86.275	94.319	59	96	
Presión de pulso	Normal	48.272	8.619	32	66	0.3852
	Sobrepeso	46.591	8.179	30	72	
	Obesidad	45.875	8.385	31	68	
Frecuencia cardiaca	Normal	82.688	9.022	61	105	0.6768
	Sobrepeso	82.172	11.856	20	113	
	Obesidad	80.725	9.336	61	102	

Fuente: Datos de la investigación.

Table 4 presents a correlation of the pressures of pregnant patients in relation to the body mass index of normal type, overweight and obesity respectively. It is observed that when the body mass of the patients increases, the diastolic and systolic blood pressures increase, unlike the pulse pressure and heart rate, which decrease when presenting greater body mass. In addition, the p value was determined using an Anova analysis of a factor for 3 levels where a significant difference was observed for diastolic and systolic pressures.

Tabla 5. Pacientes diagnosticadas con preeclampsia, candidato a desarrollar la enfermedad y pacientes normales

Número de pacientes	Porcentaje
2 Pacientes con preeclampsia.	1.14%
1 Candidato potencial.	0.57%
173 Pacientes normales.	98.29%

Fuente: Datos de la investigación.

Table 5 found that 1.14% had been detected with preeclampsia, while 0.57% represented a patient as a potential candidate to develop the disease and, 98.29% of the patients were found without data of preeclampsia.

Tabla 6. Estadísticos de las variables colesterol y triglicéridos en el 2º y 3º trimestre en las mujeres embarazadas del HGRAA

Colesterol.									
Trimestre	Media	Min	Max	DS	p95	Rango	CV	N	
2º	205.27	99	309	39.56285	279	210	0.1927278	57	
3º	242.81	146	443	51.22719	341.06	297	0.2109741	111	
Triglicéridos.									
Trimestre	Media	Min	Max	DS	p95	Rango	CV	N	
2º	209.89	80	455	75.27209	378	375	0.3586126	57	
3º	265.17	122	532	76.98628	406	410	0.2903221	111	

Fuente: Datos de la investigación.

Table 6 shows the values obtained, from pregnant patients, for the cholesterol and triglyceride variables, in which it is observed that as the trimester of pregnancy increases, the mean increases proportionally for both variables.

Tabla 7. Percentil 95 obtenidos para colesterol y triglicéridos en Argentina y contrastados con los obtenidos en México durante el 2º y 3º trimestre de la gestación.

Percentil 95						
Variable	Trimestre					
	2º		3º			
	Arg	Méx	%	Arg	Méx	%
Colesterol	290	279	3.50	321	341	6.30
Triglicéridos	257	378	21.05	371	406	8.10

Fuente: Ywaskewycz-Benítez, L. R., et al. (2010) y datos de la investigación.

Table 7 shows a comparison of 95 percentiles obtained in Argentine work and those found in this work. The percentages of Mexican individuals are observed above the cutoffs of the Argentines. The percentiles obtained in this Mexican study were higher compared to the Argentines, except for the cholesterol parameter for the second trimester of pregnancy.

Discussion

In the present study, the most frequent occupation of the patients was housewife with 79.31%. The current minimum wage in Mexico, as of January 2018, is \$ 4.32 USD per day, which gives a biweekly amount of \$ 64.8 USD, very similar to the \$ 80.93 USD that most of the patients studied declared as their income. However, the per capita income in the country is USD 8,201.31, which means that only 5.17% of patients are close to the income that each person must earn in the country, while 64.37% of patients show very low purchasing power . It also shows that the most frequent type of housing for pregnant patients is cement.

In this study, the most frequent level of schooling was secondary school with 32.1%, which agrees with the data of the Undersecretary of Employment and Productivity in Guerrero, Mexico, since it indicates that only 36.8% of the population possesses a high school degree, Similarly, the National Institute of Statistics and Geography establishes that the average population has 9.2 degrees of schooling, which means a little more than the secondary school completed.

In table 2 of biochemical parameters studied, most of them appear normal, however, in some of the alterations are detected in patients with 67.95% in urea and, with 79.55% in creatinine, which shows on average values slightly low in relation to the reference values. On the other hand, in the lipid profile shows that 69.61% of patients have relatively high values for cholesterol ranging from 99 to 443 mg / dL, likewise, 92.96% of patients have high triglyceride values ranging from 80 at 532 mg / dL.

Duarte et al., (2014), conducted a study in which they evaluated cholesterol and triglyceride levels in pregnant women, according to the severity of preeclampsia, and found that cholesterol and triglyceride levels show a considerable elevation, with values of 245 mg / dL, in both Analytes in normal pregnancy. These results are similar to the results obtained in the present study, where average cholesterol values of 229.55 mg / dL and triglycerides of 247.35 mg / dL were found.

On the other hand, the discovery of pathological values in the patients stands out: 3.58% presented abnormally high basal glucose, as well as 28.92% of the patients presented abnormal curves with the postprandial glucose.

In Table 3 of the blood count, most parameters are normal in relation to the reference values, with the exception of erythrocytes where 58.88% of the patients present a slightly low value with extreme minimum and maximum values, which go of 1.87 and 5.15 cells $\times 10^6$ / μL , in the same way, 60.55% of the patients presented low levels of hemoglobin, 5.1 being the minimum value and 15.1 the maximum value. Therefore, it can be concluded that more than 50% of the patients presented a normocytic normochromic anemia. These results are consistent with the study conducted by Celiz (2016), in which he determined that maternal anemia is a risk factor associated with preeclampsia.

Ywaskewycz et al., (2010) performed an evaluation of the lipid profile of adult women by trimester of pregnancy and compared the lipid profile of a control group of non-pregnant women, obtaining the 95th percentiles. They found that total cholesterol and triglycerides were significantly increasing during each trimester of pregnancy, these results are similar to those found in our study, where a significant increase was found during each quarter for both variables, both for cholesterol and triglycerides.

Conclusion

Of the patients, 50% belong to a population group with a fortnightly income of approximately \$ 80.93 USD, which is in accordance with the minimum wage in Mexico. Most of them have a high school level of education, equal to the national average. More than 50% of them refer to having a cement house and being in charge of the home (housewife). It was determined that 69.61% of the patients presented hypercholesterolemia and 92.26% presented hypertriglyceridemia. In addition, a directly proportional relationship was observed between the increase in body mass and pressures, both systolic and diastolic.

The results obtained show that 38.33% of the patients presented a low hematocrit, while 8.33% presented thrombocytopenia. It was detected that among the analyzed patients, 1.14% presented diagnostic criteria for preeclampsia, 0.57% were candidates to acquire the disease, and 98.29% were diagnosed as normal patients. With respect to the percentiles obtained for cholesterol and triglycerides, in this study it was found that these were higher in comparison with the Argentines, except for the cholesterol parameter during the second trimester of pregnancy.

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