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## Factors associated with pregnancy-induced hypertension in women living at high altitudes

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# FACTORS ASSOCIATED WITH PREGNANCY-INDUCED HYPERTENSION IN WOMEN LIVING AT HIGH ALTITUDES

FACTORES ASOCIADOS A HIPERTENSIÓN ARTERIAL INDUCIDA POR EMBARAZO EN PERSONAS QUE VIVEN EN ALTURA

Jenny Mendoza-Vilcahuaman<sup>1</sup>, Rossibel Juana Muñoz- De La Torre<sup>1</sup>, Anibal Valentin Diaz-Lazo<sup>2</sup>

## ABSTRACT

**Objectives:** To determine the factors associated with pregnancy-induced arterial hypertension (HIE) in people living at high altitude. **Methods:** The research was observational, cross-sectional, analytical study of cases and controls. It was held at the El Carmen de Huancayo Regional Teaching Maternal and Child Hospital, Peru located at 3,259 m.a.s.l. The calculation of the sample was Epidat 3.0. 80% power level, with frequency of 27% for cases, 17% for controls, precision of 5% and odds ratio (OR) = 2. X<sup>2</sup> squared, binomial and multivariate logistic regression were used for statistical analysis. **Results:** 960 (100%) pregnant women were included, with a mean age of 36,7 years ± 5.8 years (range: 15 to 44 years). The most frequent clinical manifestations of pregnant women with HIE were: edema (63.1%), headache (61.9%), epigastralgia (51.4%), ringing in the ears (41.9%), hyperreflexia (26.4, 2%), and scotomas (19.8%). The risk factors associated with a higher probability of HIE compared to normotensive pregnant women were: obesity (78,1% vs 39,2%); OR= 3,54; IC95: 2,31-5,42; p=0.000); scotomas (19.8% vs 4.4%; OR = 3.30; 95% CI: 1.85 - 5.91; p = 0.000), hyperreflexia (26.4% vs 2.9%; OR= 8.39; IC95%: 4.47 - 15.76; p=0.000) and extreme age (27.1% vs 17.3%; OR = 1.56; 95% CI: 1.05 - 2.319; p = 0.000). **Conclusions:** The most frequent symptoms in HIE are edema, headache and epigastric pain. The factors associated with a higher risk of HIE were obesity, scotomas, hyperreflexia and extreme age.

**Key words:** Hypertension; Pre-eclampsia; Pregnancy; Risk factors; Obesity (source: MeSH NLM).

## RESUMEN

**Ojetivos:** Determinar los factores asociados a la hipertensión arterial inducida por el embarazo (HIE) en personas que viven en la altura. **Métodos:** La investigación fue de tipo observacional, analítico de casos y controles. Se realizó en el Hospital Regional Docente Materno Infantil El Carmen de Huancayo, Perú ubicado a 3 259 m.s.n.m. El cálculo de la muestra se realizó mediante el Epidat 3.0. nivel de potencia del 80%, con frecuencia del 27% para los casos, 17% para los controles, precisión del 5% y odds ratio (OR) = 2. Para el análisis estadístico se empleó el X<sup>2</sup> cuadrado, la regresión logística binomial y multivariado. **Resultados:** Se incluyeron 940 (100%) gestantes, con promedio de edad de 36.7 años ± 5.8 años (rango: 15 a 44 años). Las manifestaciones clínicas más frecuentes de las embarazadas con HIE fueron: edemas (63,1%), cefalea (61,9%), epigastralgia (51,4%), zumbido de oídos (41,9%), hiperreflexia (26,4%), y escotomas (19,8%). Los factores de riesgo asociados a una mayor probabilidad de HIE en comparación con las embarazadas normotensas fueron: la obesidad (78,1% vs 39,2%); OR= 3,54; IC95%: 2,31-5,42; p=0.000); y edad extrema (27,1% vs 17,3%; OR= 1,56; IC95%: 1,05 - 2,319; p=0.000). **Conclusión:** Los síntomas más frecuentes en la HIE son edemas, cefalea y epigastralgia. Los factores asociados a mayor riesgo de HIE fueron la obesidad, y la edad extrema en gestantes que viven en la altura.

**Palabras clave:** Hipertensión; Preeclampsia; Embarazo; Factores de riesgo; Obesidad (fuente: DeCS BIREME).

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## INTRODUCTION

Pregnancy-induced arterial hypertension (PIH) is a pathological entity responsible for a large number of maternal morbidity and mortality worldwide. PIH is one of the most frequent complications, the main responsible for maternal mortality in the world, and occurs between 5% and 10.3% of all pregnancies<sup>(1-3)</sup>, being 1.7 times more frequent in high altitudes compared to those that live at low altitudes<sup>(4,5)</sup>.

PIH causes between 10% and 15% of maternal deaths in developing countries<sup>(6)</sup>. It also causes maternal and fetal damage, initiates vascular and metabolic alterations, which are risk factors for suffering from chronic hypertension in the future<sup>(7)</sup>. In Peru, 59.1% of maternal deaths occurred due to direct causes. The most frequent causes were hemorrhages with 25.2% and hypertensive disorders with 18.5%<sup>(8)</sup>. Risk factors associated with PIH include chronic arterial hypertension, diabetes before pregnancy, pregnant women, primiparous women, obesity, and smoking<sup>(9)</sup>.

There are no studies related to the clinical profile in pregnant women with hypertension living in high altitudes, which does not allow the optimal health of the pregnant woman and the newborn to be preserved in a timely and adequate manner. The study's objective was to determine the factors associated with PIH in people living at high altitudes.

## METHODS

### Design and study area

The research was observational, analytical of cases and controls. It was carried out at the El Carmen Regional Maternal and Child Teaching Hospital located at 3,259 meters above sea level in the province and district of Huancayo, in the department of Junín, attended from January 2017 to June 2018.

### Population and sample

The study population was made up of 1210 pregnant women who attended the El Carmen de Huancayo Regional Maternal and Child Teaching Hospital. The sample size was obtained according to Epidat 3.0, considering the statistical power level of 80%, with a frequency of 27% for cases, 17% for controls, the precision of 5%, and odds ratio (OR) = 2. The final sample consisted of 420 pregnant women diagnosed with PIH (cases) and 520 normotensive pregnant women (controls) determined with the inclusion and exclusion criteria.

**The inclusion criteria for the cases (n1) were:** patients admitted with 20 weeks of pregnancy until the beginning of labor, having a diagnosis of PIH; and for the control group (n2): patients admitted with 20 weeks of pregnancy until the beginning of labor in a normotensive condition. The exclusion criteria for pregnant women with PIH and the normotensive group were: Pregnant women in labor or scheduled for cesarean section with chronic diseases such as chronic hypertension, diabetes, kidney failure, epilepsy, heart failure, endocrine disorders, chronic infections, Tuberculosis, HIV; judicialized medical records. Simple random probability sampling was used for the selection of patients.

### Definition of variables

**Pregnancy-induced hypertension (PIH):** Recording of blood pressure values  $\geq 140/90$  mmHg in two intakes, or an increase of more than 30 mmHg in systolic blood pressure or 15 mmHg in diastolic blood pressure above normal values, after 20 weeks of pregnancy without proteinuria<sup>(10)</sup>.

**Obesity:** It was considered with a body mass index (BMI) greater than or equal to 30 Kg / m<sup>2</sup>, the BMI is the relationship between body weight (Kg) and high altitudes measured in meters squared (m<sup>2</sup>)<sup>(11)</sup>.

**Nulliparity:** It is considered to be a woman who has not yet had any childbirth<sup>(12)</sup>.

**Preeclampsia:** Presence of arterial hypertension in pregnant women after twenty weeks, with and without multiple organ dysfunction<sup>(13)</sup>.

**Eclampsia:** It is considered the pregnant woman with generalized tonic-clonic seizures, similar to epilepsy<sup>(13)</sup>.

**Twin pregnancy:** Presence of two fetuses within the same pregnancy<sup>(14)</sup>.

**Extreme age:** It is the age of the pregnant woman that includes those under 19 years of age and those over 35 years of age<sup>(15)</sup>.

### Procedures

Authorization was obtained from the Hospital, through the training, teaching, and research office to have access to the clinical records. The medical records were reviewed, the information of which was recorded in a data collection form duly validated through the judgment of experts, which numbered five, whose value was 0.9. The instrument contained general data: age, origin, weight, high altitudes, BMI, blood pressure, parity, multiple pregnancy, history

of pre-eclampsia/eclampsia, proteinuria, and signs and symptoms (headache, epigastric pain, edema, ringing in the ears, hyperreflexia, drowsiness, and scotomas). The variables were coded to create the database.

### Data analysis

Statistical analysis was performed with the SPSS 22.0 program for Windows. Categorical data were described in frequencies and percentages. The statistical test used was X<sup>2</sup> squared, binary and multivariate logistic regression, odds ratio (OR), 95% confidence interval (95% CI), and a p-value <0.05 was considered significant. For the multivariate analysis, a value of p <0.10 was included.

### Ethical aspects

Authorization was obtained from the Directorate of

the Research Institute of the National University of Huancavelica to carry out the research work. The data was handled with the reserve and confidentiality of the case being only used for investigation purposes anonymously.

## RESULTS

940 pregnant women were included, with a mean age of 36.7 years ± 5.8 years (range: 15 to 44 years). Table 1 shows the symptoms present in pregnant women with PIH compared to normotensive pregnant women, such as edema (63.1% vs 26.9%); headache (61.9% vs 25.8%); epigastralgia (51.4% vs 24.6%); ringing in the ears (41.9% vs 23.7%), hyperreflexia (26.4% vs 2.9%) and scotomas (26.1% vs 20.8%).

**Table 1.** Clinical profile of pregnant women with pregnancy-induced hypertension and normotensive pregnant women living at high altitudes.

Signs and symptoms	Gestantes				P-value
	Hypertensive 420		normotensive 520		
	n	%	n	%	
Ageextreme	114	27.1	90	17.3	<0.001
Edema	265	63.1	140	26.9	<0.001
Headache	260	61.9	134	25.8	<0.001
Epigastralgia	216	51.4	128	24.6	<0.001
Tinnitus	176	41.9	123	23.7	<0.001
Hyperreflexia	111	26.4	15	2.9	<0.001
Somnolence	110	26.1	108	20.8	0.050
Scotomas	83	19.8	23	4.4	<0.001

**Source:** Data collection sheet on the clinical profile of pregnancy-induced hypertension in a Regional Maternal and Child Teaching Hospital El Carmen.



**Table 2.** Factors associated with pregnant women with pregnancy-induced hypertension living in high altitudes.

Associated factors	Pregnant women				p-value
	PIH		Normotensive		
	n	%	n	%	
Nulliparity	280	66.6	373	71.7	0.09
Obesity	328	78.1	204	39.2	<0.001
twin pregnancy	16	3.8	35	6.7	0.049
History of preeclampsia/eclampsia	235	55.9	109	20.9	<0.001
Proteinuria > 300 mg / 24 h	29	6.9	9	1.7	<0.001
Ringing in the ears	176	41.9	123	23.7	<0.001
Hyperreflexia	111	26.4	15	2.9	<0.001
Drowsiness	110	26.1	108	20.8	0.050
Scotomas	83	19.8	23	4.4	<0.001

ORIGINAL PAPER

**Source:** Overview of data collection on the clinical profile of pregnancy-induced hypertension at Hospital Regional Teaching Materno Infantil El Carmen.

**PIH:** Pregnancy-induced hypertension.

Table 2 shows the factors associated with pregnancy-induced hypertension in comparison with normotensive pregnant women; such as obesity (78.1% vs. 39.2%;  $p = 0.000$ ); History of pre-eclampsia or eclampsia (55.9% vs. 20.9%;  $p < 0.001$ ),

and proteinuria greater than 300 mg in 24 hours (6.9% vs 1.7%;  $p < 0.001$ ) presented a significantly higher probability of PIH ; that is, all these factors presented a value of  $p < 0.05$ .

**Table 3.** Multivariate analysis of the factors associated with pregnant women with pregnancy-induced hypertension living in high altitudes.

Associated factor	P-value	adjusted OR	95% CI
Extreme age	0.000	1.91	1.36-2.68
Pregnancy	0.089	0.56	0.29-1.08
Obesity	0.000	3.87	2.68-5.58
History of preeclampsia	0.157	1.30	0.90-1.89

**Source:** Sheet clinical data collection profile induced hypertension pregnancy at El Carmen Regional Maternal and Child Teaching Hospital.

In the multivariate analysis, the factors positively associated with high-altitude pregnancy-induced hypertension were: extreme age (OR = 1.91; 95%

CI: 1.36 - 2.68) and obesity (OR = 3.87; 95% CI: 2.68 - 5.58), while twin pregnancy and a history of pre-eclampsia were not associated with PIH.

## DISCUSSION

Pregnancy-induced hypertension has a negative impact on perinatal maternal health with an as yet unknown origin. Symptoms associated with pregnancy-induced hypertension were hyperreflexia and scotomas, results that differ from previous studies where they identified the same symptoms for PIH<sup>(12,14)</sup>; likewise, Lloret<sup>(16)</sup> emphasizes the presence of the clinical triad basic conformed by arterial hypertension, edema, and proteinuria. However, Pacheco<sup>(17)</sup> points out that hypertensive disease is a common factor in increased blood pressure.

Persistent headache, temporary or permanent visual disturbances and epigastric pain can be prodromal symptoms of eclampsia. Epigastralgia is caused by distention of Glisson's capsule due to ischemia, necrosis, and hepatocellular edema; Given these symptoms in mild/moderate pre-eclampsia (PE), it is necessary to think that the evolution to severe pre-eclampsia is possible<sup>(18)</sup>.

These results were found in pregnant women living in high altitudes who present diverse symptoms. Therefore they have a higher risk of maternal-fetal complications with a risk of mortality; These results compared to the literature, we would be facing an evolution of severe pre-eclampsia.

On the other hand, extreme age is associated with pregnancy-induced hypertension, results that agree with the study of Cashew<sup>(19)</sup>, who found that age less than or equal to 19 years (OR = 3.4) and age greater than or equal to 35 years (OR = 2.0) both with increased risk of suffering from this pathology. Several authors agree that, in women under 19 years of age, the risk of pre-eclampsia doubles, and they have suggested that women over 35 years of age have a higher risk of suffering from pre-eclampsia because they suffer more frequently from chronic vascular diseases and that facilitates the emergence of hypertensive diseases of pregnancy and preeclampsia<sup>(20)</sup>. These results are similar due to the sociodemographic context in which the study is developed, and extreme age populations are susceptible to suffering from this pathology. There is a poor adaptation to the vascular tree of the uterine muscle imposed by pregnancy at this age.

Factors positively associated with pregnancy-induced hypertension were extreme age and obesity.

These results are different from those of Enriquez<sup>(21)</sup>, who found that the main risk factors associated with induced hypertension of pregnancy were; personal history of PIH (OR = 78.00); family history of PIH (OR = 42.75) and overweight (OR = 1.44); Likewise, Hernández<sup>(22)</sup>, reported as factors associated with PIH, the maternal history of PIH (OR = 5.21; 95% CI: 1.75-15.85;  $p = 0.002$ ), inadequate prenatal controls (OR = 2.77; 95% CI: 6.89-23.80;  $p = 0.026$ ), and nulliparity (OR = 2.72; 95% CI: 1.15-6.39;  $p = 0.020$ ). Likewise, the studies by Sucksdorf<sup>(23)</sup> and Fuentes<sup>(24)</sup> affirm that nulliparity is a risk factor for hypertensive disorders in pregnancy. Other investigations such as the one carried out by Rojas<sup>(25)</sup> at the Vitarte Hospital and the one by Álvarez<sup>(26)</sup> at the Hipólito Unanue Hospital found an association between nulliparity and PIH with an OR = 2.56 and OR = 5.70 respectively. The reports above do not agree with the findings of our study.

Obesity was another positively associated factor, in this regard, Álvarez<sup>(26)</sup> emphasizes that the risk of obesity and pregnancy-induced hypertension is two times more (OR = 2.33), Arroyo<sup>(27)</sup> reports an OR of 1, 99 and Flores<sup>(28)</sup> conclude that a body mass index greater than 25 Kg / m<sup>2</sup> is an associated factor. Obesity is characteristic of tall women, the product of a consumer society (sedentary lifestyle, hypercaloric and hyper fat diet), increasing the risk of cardiovascular diseases associated with a higher level of oxidative stress with endothelial dysfunction.

The findings showed that pregnant women who lived at high altitudes and were obese were between 2 and 5 times more likely to suffer from PIH, so the actions to be taken should control this factor.

A limitation of the study was the small population included in the study; the data obtained was from the medical records, which could contain some information bias, so the generalization of the results should be taken with caution.

## CONCLUSION

It is concluded that the most frequent symptoms in PIH are edema, headache, and epigastric pain. The factors associated with a higher risk of PIH were extreme age and obesity in pregnant women living at high altitudes, increasing perinatal maternal mortality.



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