## **ORIGINAL ARTICLE**

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# Risk of preeclampsia in adolescent primigravidae in a hospital in the Junin region of the Peruvian highlands

Riesgo de preeclampsia en primigestas adolescentes en un hospital de la región de Junín en la sierra peruana

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#### **ABSTRACT**

Introduction: Preeclampsia is one of the main causes of morbidity and mortality in the world and in Peru. The role of adolescent pregnancy in the development of preeclampsia is not clear. Objectives: To analyze the risk of preeclampsia in pregnant adolescent primigravidae in a maternal and child hospital in the Peruvian highlands. Methods: Analytical retrospective cohort study. Pregnant women attended between 2018 and 2021 at the Hospital Regional Docente Materno Infantil "El Carmen", in Junín, Peru, were included. A Poisson regression model adjusted for theoretical and epidemiological criteria was used, calculating the relative risk (RR). Results: A total of 504 primigravidae were included, 35.9% were adolescents aged 10-19 years and 64.1% were adults. A non-significant higher incidence of preeclampsia was observed in adolescents (7.2%) than in adult pregnant women (3.4%) (RR 1.77; 95% CI 0.76-4.14; p 0.19). Conclusion: No association was found between adolescent pregnancy and the development of preeclampsia in a maternal and child hospital in the Peruvian

Key words: Pregnancy in adolescence, Pre-eclampsia, Pregnancy-induced hypertension

#### **RESUMEN**

Introducción. La preeclampsia representa una de las principales causas de morbimortalidad en el mundo y el Perú. El rol del embarazo adolescente en el desarrollo de preeclampsia no es claro. Objetivos. Analizar el riesgo de preeclampsia en primigestas adolescentes embarazadas en un hospital materno infantil de la sierra peruana. Métodos. Estudio analítico de cohorte retrospectivo. Se incluyeron gestantes atendidas entre el 2018 y 2021 en el Hospital Regional Docente Materno Infantil "El Carmen", en Junín, Perú. Se utilizó un modelo de regresión de Poisson ajustado por criterio teórico y epidemiológico, calculando el riesgo relativo. Resultados. Se incluyeron 504 primigestas, 35,9% fueron adolescentes de 10 a 19 años y 64,1% adultas. Se observó una mayor incidencia no significativa de preeclampsia en adolescentes (7,2%) que en gestantes adultas (3,4%) (RR 1,77; IC 95% 0,76 a 4,14; p 0,19). Conclusión. No se encontró una asociación entre el embarazo adolescente v el desarrollo de preeclampsia en un hospital materno infantil de la sierra peruana. Palabras clave. Émbarazo en adolescencia, Preeclampsia, Hipertensión inducida en el embarazo

## INTRODUCTION

Pregnancy between 10 and 19 years of age, defined as adolescent pregnancy, is associated with limitations in education, information and even sexual freedom<sup>(1)</sup>. Latin America and the Caribbean have the second highest rate of teenage pregnancy in the world, while Peru has a rate of 56.9 births per 1,000 women between 15 and 19 years of age<sup>(2)</sup>. According to the Demographic and Family Health Survey (ENDES, by its acronym in Spanish), 8.9% of adolescents have ever been pregnant, especially in rural areas and low-income groups<sup>(3)</sup>.

Hypertensive disorders of pregnancy are responsible for 14% of maternal deaths worldwide(4,5). In Peru, they represented the second leading cause of maternal death in the period 2017 - 2018 and the first overall cause of death between 2000 and 2010(6,7). In the Hospital Regional Do-



cente Materno Infantil "El Carmen" hypertensive disorders of pregnancy were included among the first 10 causes of maternal morbidity during 2021<sup>(8)</sup>.

The risk factors for the development of preeclampsia include nulliparity, obesity, endothelial dysfunction and maternal age extremes<sup>(9-11)</sup>. Because of the controversy surrounding the development of preeclampsia in adolescents, The American College of Obstetricians and Gynecologists (ACOG) does not include it as a risk factor<sup>(12)</sup>.

Junín department is located in the central area of the Peruvian Andes, where one fifth of the population lives in poverty<sup>(13)</sup>. To our knowledge, there are no studies that have investigated the association between adolescent pregnancy and the development of preeclampsia in the Peruvian highlands. The main objective of this study is to investigate the risk of adolescent pregnancy in the development of preeclampsia in primigravidae in the Peruvian highlands, to describe the incidence of preeclampsia in this population and to evaluate other possible associated factors.

#### **METHODS**

This retrospective cohort study was conducted at the Hospital Regional Docente Materno Infantil "El Carmen" located in Junín, Peru, a category II-E facility in the Peruvian highlands, where approximately 27.8% of women live in poverty<sup>(14)</sup>. This facility serves the population of the province of Huancayo and the Central Macro Region.

The Junín region is located 3,259 meters above sea level in the central zone of the Peruvian Andes, whose primary economic activity is the extraction of oil, gas and minerals, as well as agriculture, livestock and forestry<sup>(13)</sup>.

The population studied consisted of primigravid women attended at the Hospital Regional Docente Materno Infantil "El Carmen" during the years 2018 to 2021. In 2021, 11,334 medical attentions and 1,784 deliveries were recorded. The study comprised primigravid patients aged 10 to 35 who received prenatal care before 20 weeks, had blood pressure readings within normal ranges and gestational ages greater than 20 weeks, were included. Women with multiple

gestation or with a history of diabetes mellitus, arterial hypertension or familial preeclampsia were excluded.

The EPIDAT program was used to calculate the sample size, based on a previous similar study<sup>(15)</sup>. Approximately 11.6% of adolescent pregnant women with preeclampsia were considered, compared with 3.7% of adult pregnant women. An unexposed/exposed ratio of 4, power of 80%, and confidence level of 95% were included. In addition, we estimated an approximate 11% of incorrectly completed histories or incomplete data. Thus, a minimum sample size of 534 participants was calculated. Consecutive, non-probabilistic sampling was used.

The independent variable was age, being a dichotomous categorical variable: adolescents (10-19 years) and adults (20-35 years)<sup>(16)</sup>. The dependent variable was the development of preclampsia, defined as blood pressure greater than 140/90 mmHg on at least two occasions, from 20 weeks of gestation in previously normotensive patients and proteinuria greater than or equal to 300 mg in 24 hours<sup>(17)</sup>.

In addition, sociodemographic characteristics were recorded, such as age (years), marital status (single, married or cohabiting), educational level (illiterate/primary, secondary or higher), place of origin (Junín or other regions) and body mass index - BMI (adequate, underweight and overweight/obese). On the other hand, clinical variables such as number of prenatal controls, proteinuria (mg/dL), alcohol or tobacco consumption, urinary tract infection (UTI), type of delivery (vaginal or cesarean) and gestational age at delivery (in weeks) were considered.

The information was recorded and coded in Excel, and subsequently imported into the STATA v.16.0 program for analysis. Categorical variables (sociodemographic and clinical) are presented as percentages. The numerical variables had a non-normal distribution (Shapiro-Wilk test), so the median with interquartile range was used as a summary measure.

The bivariate analysis was performed as follows: chi-square was used for categorical variables and the Mann Whitney U non-parametric test was used for the analysis of non-numerical variables.



Regarding the multivariate analysis, the independent variables that showed significance in the crude analysis together with the variable 'urinary tract infection' were selected by theoretical criteria. The Poisson regression model adjusted for confounding variables was used to calculate the relative risk (RR). To assess statistical significance, a value of p<0.05 was established and a 95% confidence interval (CI) was calculated for each test performed.

The present study was approved by the Ethics Committee of the Faculty of Health Sciences of the Universidad Peruana de Ciencias Aplicadas (Approval number: FCS.SCEI/050-01-23) and the Hospital Docente Materno Infantil "El Carmen" for access to clinical records. No interventions were performed on study participants and no personally identifiable patient data were included. The data collected were entered into a database, to which only the researchers had access.

In addition, no technology related to artificial intelligence was implemented in any collection, analysis, or writing process.

#### RESULTS

A total of 504 primigravidae were included, of which 181 (35.9%) were adolescents and 323 (64.1%) were adults (Table 1). Thirty-two percent of the adolescent pregnant women were single and 2.2% were married, compared to 20.4% and 6.8% of the adult pregnant women. Of the adolescent pregnant women, 51.4% were illiterate or had only primary school education. Compared to adolescent pregnant women, a greater proportion of adult pregnant had overweight and obesity (31.0% vs. 17.1%). The median systolic blood pressure (SBP) and diastolic blood pressure (DBP) in both groups were equivalent before and after 20 weeks of gestation.

Regarding other risk factors, tobacco use was more frequent in adolescents (2.2%) compared to adults (0.6%). In addition, adolescents had a slightly higher percentage of urinary tract infections (17.7%) compared to adults (14.2%) (Supplementary material).

A non-significant higher incidence of preeclampsia was observed in adolescent pregnant women (7.2%) than in adult pregnant women (3.4%) (Ta-

TABLE 1. SOCIODEMOGRAPHIC CHARACTERISTICS OF THE PREGNANT WOMEN (N = 504).

Variables	Adolescents (n =181)	Adults (n = 323)	
Variables	n (%)	n (%)	
Age (years)*	17 (16 - 18)	24 (22-27)	
Marital status			
Single	58 (32.0)	66 (20.4)	
Married	4 (2.2)	22 (6.8)	
Cohabitant	119 (65.8)	235 (72.8)	
Education level			
Illiterate / elementary school	93 (51.4)	22 (6.8)	
High school	88 (48.7)	219 (67.8)	
Higher education	0 (0)	82 (25.4)	
Place of origin			
Junín	178 (98.3)	317 (98.1)	
Other region	3 (1.7)	6 (1.9)	
Nutritional status			
Appropriate	138 (76.2)	216 (66.9)	
Underweight	12 (6.6)	7 (2.2)	
Overweight and obesity	31(17.1)	100 (31.0)	
Size (m)*	1.51 (1.48 – 1.55)	1.52 (1.49-1.56)	
Weight (kg)*	50 (46 – 56)	54 (50-60)	
BMI (kg/m2)*	22.1 (20.3 – 23.8)	23.3 (21.6 - 25.9)	
Preeclampsia	13 (7.2)	11 (3.4)	
Alcohol consumption	1 (0.6)	2 (0.6)	
Tobacco use	4 (2.2)	2 (0.6)	
UTI	32 (17.7)	46 (14.2)	
Type of delivery			
Vaginal	104 (57.5)	143 (44.3)	
Cesarean section	77 (42.5)	180 (55.7)	
Gestational age at delivery (weeks)*	39 (37 – 40)	39 (38-40)	
SBP ≤ 20 weeks (mmHg)*	95 (90 – 100)	100 (90-100)	
DBP ≤ 20 weeks (mmHg)*	60 (60 – 60)	60 (60-60)	
SBP > 20 weeks (mmHg)*	110 (100 – 117)	110 (100-111)	
DBP > 20 weeks (mmHg)*	70 (60 – 70)	70 (60-70)	
Number of prenatal checkups*	6 (4- 8)	7 (5-8)	

BMI: body mass index, UTI: urinary tract infection, SBP: systolic blood pressure, DBP: diastolic blood pressure

ble 2). Pregnant women with low birth weight developed more preeclampsia (15.8%) than those with adequate nutritional status (4.8%). No significant differences were found in the incidence of preeclampsia and marital status, nutritional status, educational level, BMI value.



TABLE 2. SIMPLE (CRUDE) AND ADJUSTED (MULTIPLE) REGRESSION ANALYSIS OF FACTORS ASSOCIATED WITH PREECLAMPSIA AND ADOLES-CENCE.

Varia-	Crude analysis		Adjusted analysis			
bles	RR	CI 95%	p-Value	RR	CI 95%	p-Value
Age group						
Adults	1			1		
Adoles- cents	2.1	0.96 – 4.61	0.06	1.77	0.76 – 4.14	0.19

Poisson regression adjusted for age group RR: relative risk, CI: confidence interval

## DISCUSSION

Although preeclampsia was shown to be more common in teenage pregnant women than in adult women, there was no statistically significant difference in the incidence of the condition.

These results coincide with a study conducted in Zambia<sup>(18)</sup>, where pregnant women between 10 and 19 years of age had a 36% higher risk of developing preeclampsia compared to patients between 20 and 24 years of age, although the difference was not significant. However, in the same study it was found that pregnant women between 25 and 34 years of age had a higher risk of preeclampsia compared to adolescents. It is important to mention that both multiparous and primiparous women were included, which have a higher risk of preeclampsia<sup>(9)</sup> and may represent a bias in these results.

Similarly, a study conducted in the United States found that younger adolescents were at higher risk of developing preeclampsia<sup>(19)</sup>. Patients under the age of 15 were considered in this study as younger adolescents. This may suggest a probable inversely proportional relationship between the risk of preeclampsia and the age of the pregnant woman.

This possible increased risk in adolescent pregnant women may be explained by uterine immaturity in very young pregnant women. Inadequate uterine development is associated with placental insufficiency due to defective remodeling of the vasculature or uterine overdistension and subsequent release of inflammatory mediators(20,21).

Contradictorily, a study carried out in Bogotá, which included nulliparous patients between 10 and 29 years of age found adolescent pregnancy to be a protective effect for the development of preeclampsia<sup>(22)</sup>.

SUPPLEMENTARY MATERIAL 1. COMPARISON OF SOCIODEMOGRAPHIC AND CLINICAL CHARACTERISTICS BETWEEN PATIENTS WITH AND WITHOUT PREECLAMPSIA.

	Preeclar			
Variables	Yes	No	p - Value	
	n (%)	n (%)		
Age group**				
Adolescent	13 (7.2)	168 (92.8)	0.056	
Adult	11 (3.4)	312 (96.6)		
Age*	19 (17.5 – 24.5)	21 (18 – 25)	0.134	
Marital status**				
Single	3 (2.4)	121 (97.6)	0.330	
Married	1 (3.9)	25 (96.2)	0.339	
Cohabitant	20 (5.7)	334 (94.4)		
Education level**				
Illiterate / elementary school	9 (7.8)	106 (92.2)	0.096	
High school	14 (4.6)	293 (95.4)		
Higher education	1 (1.2)	81 (98.8)		
Size* (cm)	1.5 (1.5 – 1.6)	1.5 (1.5 – 1.6)	0.075	
Weight* (kg)	53.5 (48 – 57)	53 (48 – 59)	0.613	
BMI* (kg)	22.7 (20.2 – 23.8)	22.8 (21.1 – 25.3)	0.199	
Nutritional status**				
Appropriate	17 (4.8)	337 (95.2)	0.051	
Underweight	3 (15.8)	16 (84.2)	0.051	
Overweight and obesity	4 (3.1)	127 (97.0)		
Number of prenatal checkups*	7 (5.0 – 8.0)	6 (5.0 – 8.0)	0.631	
Tobacco consumption**				
No	22 (4.4)	476 (95.6)	0.029	
Yes	2 (33.3)	4 (66.7)		
UTI**				
No	21 (4.9)	405 (95.1)	0.476	
Yes	3 (3.9)	75 (96.2)		

\*Mann-Whitney U test. \*\*Chi-square. BMI: body mass index. UTI: urinary tract infection.

As shown, most studies conclude that adolescence is a risk factor for the development of preeclampsia. Some have statistical significance and others do not, as in our study, which may be related to the sample size or primiparity as an inclusion criterion.

Additionally, a prospective study performed in countries from different continents suggests that adolescent pregnancy is associated with worse perinatal outcomes, especially with biological immaturity and socioeconomic factors<sup>(23)</sup>. In addition, the incidence of preeclampsia tends to be higher in lower-income countries(24). Although maternal outcomes may be independent



of maternal age<sup>(25)</sup>, the risk of preeclampsia represents an important additional factor in possible neonatal outcomes in the adolescent population(26).

The variation in our results compared with those in the literature may be associated with the effects of altitude. Although not clearly established as a risk factor, elevated blood pressure levels have been observed in areas of higher altitude(27), which could represent a potential risk associated with a higher incidence of preeclampsia<sup>(28)</sup>. Physiological changes have been identified in pregnant women exposed to altitude and hypobaric hypoxia, which is associated with a decrease in vasodilators such as nitric oxide due to high hemoglobin concentration and a risk of defective vascular alteration, as well as reduced blood flow with inadequate supply to the uteroplacental unit<sup>(29)</sup>.

Regarding the association between the nutritional status of the pregnant woman and the development of preeclampsia, our results indicate that underweight patients have 2.45 times the risk of developing preeclampsia. However, no statistical significance was obtained, similar to that found in the literature, where Alvarez and collaborators (30) found a 60% higher risk of preeclampsia in patients with low weight, without statistical significance.

When analyzing these results, it should be considered that the Junin region has a high rate of low weight in Peru<sup>(31)</sup>, and this is associated with nutritional deficiencies in the diet. There is a possible association between vitamin, iron, folic acid and omega-3 deficiencies and an increased risk of preeclampsia(32).

Despite these findings, most studies associate obesity as a risk factor with the development of preeclampsia during gestation(33). In addition, an evaluation in Florida found that adolescents with obesity had approximately four times the risk of developing preeclampsia and eclampsia compared with non-obese adult pregnant women<sup>(34)</sup>, possibly because of the combined risk of adolescent pregnancy and obesity.

Adolescent pregnancy is a problem in which social, economic and cultural factors must be considered. In Junin, the percentage of underweight

pregnant women is very high, at 11.9%(32). Thus, within the population studied, weight gain may be associated with a lower risk of developing preeclampsia.

In rural places, adolescent pregnancy -especially among younger adolescents- is a serious issue. It restricts their access to education, increases their chance of dropping out of school, and frequently gives to fears of violence and rights violations<sup>(35)</sup>. For this reason, we highlight the importance of associations such as the working subgroup "Maternal and Neonatal Health and Prevention of Adolescent Pregnancy" of the round table for the fight against poverty<sup>(36)</sup>.

Although adolescent pregnancy remains a problem, especially in developing countries, economic security and equitable access to basic health services have an important impact on birth outcomes, reducing negative maternal and neonatal outcomes among nulliparous adolescents<sup>(37)</sup>. In vulnerable populations - such as adolescent pregnant women - these factors should be included in policies aimed at reducing complications of preeclampsia.

The present study has limitations. Firstly, with regard to external validity, it should be considered that the study was carried out in a population from the Peruvian highlands, which should be considered when extrapolating the results to a population with different sociodemographic characteristics. Secondly, it was not specified whether tobacco consumption was before or during pregnancy, in addition to a measurement bias because it was not adequately reported in the clinical histories. Third, due to the research methodology, there is the possibility of limitations in the quality or completeness of the information in the medical records, even though they were filled out by qualified health personnel.

Given the limitations, we also highlight the strengths. The ACOG criteria were used when making the diagnosis of preeclampsia, ensuring an accurate diagnosis. In addition, unlike most studies in the existing literature, only nulliparous women were included, which ensures homogeneity of the sample and more specific exploration of associated factors in the population studied.



#### CONCLUSIONS

According to our results, adolescent pregnancy, despite having a higher incidence, was not associated with a higher risk of developing preeclampsia in the population of the Peruvian highlands studied.

For future research, prospective studies with larger samples should be carried out, including decentralized centers. In addition, taking primiparity into account, it is possible that younger adolescents are at a higher risk. It is suggested to concentrate community efforts on creating interventions meant to prevent teenage pregnancy.

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