

Maternal overweight and obesity before pregnancy as predictors of childhood asthma in children under five years: a retrospective cohort in Peru

Victor Oviedo-Carquin ¹

 <https://orcid.org/0000-0002-5350-0397>

Percy Herrera-Añazco ⁴

 <https://orcid.org/0000-0003-0282-6634>

Cristhian Hajar-Zevallos ²

 <https://orcid.org/0000-0003-1658-0639>

Diego Urrunaga-Pastor ³

 <https://orcid.org/0000-0002-8339-162X>

^{1,2,4} School of Medicine. Universidad Peruana de Ciencias Aplicadas. Av Prolongacion Primavera 2390, Monterrico Santiago De Surco. Lima, Peru.
Email: silamud@gmail.com

³ Departamento de Medicina Humana. Facultad de Ciencias de la Salud. Universidad Científica del Sur. Lima, Peru.

Abstract

Objectives: to estimate the role of maternal overweight and obesity before pregnancy as predictors of childhood asthma in a population of Peruvian children under five years.

Methods: we carried out a retrospective cohort study of children aged five years or less and their mothers from the Regional Hospital of Ayacucho and the María Auxiliadora Hospital in Lima, Peru. We included children who were born between 2013 and 2014 and follow them up until 2018 and 2019, respectively. The diagnosis of overweight and obesity of the mother before pregnancy and asthma in the child were registered in their clinical histories. Crude (cRR) and adjusted relative risks (aRR) and 95% confidence intervals (CI95%) were obtained using a generalized lineal model of the Poisson family with link log and robust variances.

Results: we evaluated 431 medical records and found that 20.9% of the children had asthma, 26.7% of the mothers were overweight, and 20.2% were obese before pregnancy. In the adjusted regression model, overweight (aRR=2.94; CI95%= 1.54-5.60) and maternal obesity (aRR=5.10; CI95%= 2.73-9.51) were predictors of an increased risk of childhood asthma.

Conclusions: maternal overweight and maternal obesity increased the risk of her children developing asthma three- and five-fold, respectively.

Key words Asthma, Overweight, Obesity, Child, Pregnancy



Introduction

Overweight and obesity are multifactorial chronic conditions due to changes in lifestyle.¹ Both conditions are considered a public health problem and in the case of obesity, the prevalence tripled between 1975 and 2016, affecting more than 650 million adults worldwide in 2016.² According to a study carried out in 2019, in Peru, 20.6% of the female population over the age of 18 was obese.³ Overweight and obesity are a health problem in women of reproductive age and even affect pregnant women.⁴ In our country, a study carried out by the National Center for Food and Nutrition showed that more than half of the Peruvian women evaluated during the years 2009 and 2010 were overweight or obese at the beginning of their pregnancy.⁵

In pregnant women, overweight and obesity are related to arterial hypertension, gestational diabetes, miscarriage, intrauterine fetal death, fetal macrosomia, and increased maternal and fetal mortality.⁶ In addition, they are related to an increase in inflammatory markers such as cytokines and adipokines which, in the long term, cause physiological modifications leading to alterations in respiratory function due to the proinflammatory state and can condition the appearance of respiratory diseases in their children.⁷⁻⁹

Respiratory diseases are common in pediatrics, with asthma being the most common chronic disease in childhood.¹⁰⁻¹¹ Childhood asthma is a chronic inflammatory disease of the airways that produces recurrent episodes of wheezing, dyspnea, and dry cough.⁹ In the United States, asthma affects approximately 6.8 million children, which causes a considerable burden of hospitalizations and an estimated loss of 13.8 million days annually due to the management of patients who suffer from it.¹²⁻¹³ Other data show the overall highest prevalence in the Puerto Rican population (17.0%) and the lowest prevalence in the Mexican American population (3.9%).¹³ In Peru, it is estimated that 20% of the child population has this disease, which makes Peru the country with the highest prevalence of childhood asthma in Latin America.¹⁴ The main risk factors associated with childhood asthma are male gender, family history, and allergies.¹⁵ Additionally, it is suggested that maternal overweight and obesity could also be risk factors for this disease.¹⁶ Obesity is associated with increased respiratory effort and impaired functional lung capacity, as well as a systemic proinflammatory state with increased cytokines and chemokines, being especially of note in women due to the bronchoconstrictive action of the aromatase enzyme.¹⁶⁻¹⁹ In this sense, a systematic review of 145,574 mother-child pairs suggested that both maternal overweight and obesity before pregnancy increase the risk of children presenting childhood asthma

and wheezing. However, no study has included Hispanic mothers and children as a sample.²⁰ Taking into account that according to the World Health Organization (WHO) the Hispanic ethnic group has a higher prevalence of obesity and childhood asthma, we considered it necessary to evaluate this possible association in our population in order to identify possible potentially preventable risk factors against the development of childhood asthma.²¹ Therefore, the objective of this research was to estimate the role of maternal overweight and obesity before pregnancy as predictors of childhood asthma in a population of Peruvian children under five years.

Methods

We developed a retrospective cohort study. The population was children under five years of age and their mothers from the María Auxiliadora Hospital in Lima and the Ayacucho Regional Hospital. We included children who were born between 2013 and 2014 and follow them up until 2018 and 2019, respectively. We excluded children and the mothers with incomplete medical records or those that did not have the variables of interest, as well as children with medical histories of lung disease, cancer, human immunodeficiency virus infection, or congenital and genetic diseases.

We estimated the sample size considering the incidence of asthma in children of mothers who were not overweight before pregnancy and of mothers who were overweight before pregnancy (49.8% and 26.4% respectively).²⁰ A power of 80% and a confidence level of 95% were considered. The final calculated sample size was 143 mother-child pairs. A percentage of data loss from medical records of 30% was considered, for which the final sample size was 204.

The outcome variable was the diagnosis of childhood asthma made by a pediatrician and recorded in the medical record using the ICD-10 code J45. In these hospitals, diagnosis is based on a parental history of atopic disease (asthma or atopic dermatitis), a history of atopic disease (recurrent episodes of wheezing, coughing, shortness of breath, and chest tightness), a physical examination confirming obstruction of the respiratory tract and the absence of an alternative explanation.^{22,23}

The exposure variable was maternal body mass index (BMI) prior to pregnancy recorded in medical records. Overweight and obesity were defined if the mother had a BMI between 25 and 30 kg/m² and greater than 30 kg/m², respectively.

In addition, the following variables were collected: age and sex of the child, age of the mother, area of residence (coast, mountains, jungle) and educational level of the mother (primary, secondary, and higher).

Likewise, gestational age was considered (premature with less than 37 weeks, at term between 37 to 41 weeks and post term with more than 41 weeks) and birth weight (extremely low weight with less than 1000 g, very low weight with less than 1500 g, low weight with less than 2500 g, insufficient birth weight between 2500 and 2999 g, normal weight between 3000 and 4000 g and macrosomia with more than 4000 g). Prematurity was also included if the child was born before 37 weeks, as well as the type of delivery (natural or cesarean section) and the APGAR score at 5 minutes after birth (severe depression from 0-3, moderate depression from 4-6 and normal if was from 7-10). Additionally, the Silverman and Anderson Test was evaluated at birth (without respiratory distress if the score was 0, mild respiratory distress from 1-3, moderate respiratory distress from 4-6 and severe respiratory distress from 7-10); the family history of atopy in the child and the time of diagnosis of childhood asthma (0-12 months, 1-2 years, and 2-5 years). The age of the first childhood asthma attack (0-12 months, 1-2 years, and 2-5 years) and the number of childhood asthma attacks in the last year (0-5 attacks, 5-10 attacks and 10 or more attacks) were also evaluated.

Other variables were a maternal family history of diabetes, arterial hypertension, and cardiovascular disease; if the pregnant woman presented any respiratory disease during pregnancy and the consumption of harmful substances (tobacco, alcohol, drugs, or none) recorded in her medical history.

Data in the Excel program was exported to STATA v17.0 software (College Station Stata Corp). For the description of numerical variables, we presented means and standard deviation or medians and interquartile ranges, as appropriate. For the categorical variables, we calculated frequencies and percentages.

We used Chi-square and Fisher exact tests for the bivariable analysis comparing categorical variables. For the comparison of mean/medians between two groups, we used the Student's-t and Mann Whitney U tests, as appropriate.

For the multivariable analysis, we used a generalized linear model of the Poisson family with logarithmic link function and robust variances to estimate the relative risk (RR) with their respective 95% confidence intervals (CI95%) of the association of interest. We performed two models, one crude and the other adjusted for potential confounders. Likewise, we evaluated the assumptions of the chosen regression model, as well as collinearity problems. Values of p less than 0.05 were considered significant.

This study was approved by the Ethics Committee of the Peruvian University of Applied Sciences with approval number FCS-CEI 572-07-2 and permission to

access information from the Maria Auxiliadora Hospital and the Regional Hospital of Ayacucho.

Results

We evaluated 431 clinical histories of children: 66.8% being boys. The histories of the children showed that 10.4% were premature and 18.6% had a family history of atopy. Among the mothers, 26.7% were overweight and 20.2% were obese. The rest of the characteristics are shown in Table 1.

In the bivariable analysis of the characteristics of the children and the BMI categories of the mothers, we found a significant association with gestational age, birth weight, prematurity, the APGAR score at 5 minutes, the Silverman Anderson score, the family history of atopy, age at first asthma attack, and number of attacks in the last year (Table 1). Similarly, in the bivariable analysis of the general characteristics of the children according to the incidence of childhood asthma, there was a significant association with gestational age, birth weight, prematurity, the APGAR at 5 minutes, the Silverman Anderson score, the family history of atopy, the age of the first asthmatic attack and the number of attacks in the last year (Table 2).

In the crude multivariable analysis, we found that overweight (cRR=8.56; CI95%= 4.46-16.42) and maternal obesity (cRR=9.74; CI95%= 5.06 -18.73) were predictors of an increased risk of childhood asthma incidence (Table 3). This association was maintained in the adjusted analysis after including confounding variables such as child sex, age, prematurity, type of delivery, family history of atopy, and mother age tertiles, both in the case of overweight (aRR=2.94; CI95%= 1.54-5.60) and maternal obesity (aRR=5.10; CI95%= 2.73-9.51) (Table 3).

Discussion

The main finding of our study was that maternal overweight and obesity before pregnancy increased the risk of the children developing asthma by almost three- and five-fold, respectively. Although with some methodological and sociodemographic differences, other studies have described similar results. Research in Danish children found that maternal obesity during pregnancy was associated with an increased risk of asthma and wheezing in children.²⁴ Similarly, in the Netherlands, another study found that children with a predisposition to asthma may have an increased risk of developing the disease during childhood if their mothers were overweight before pregnancy.²⁵ Another study also conducted in Dutch children concluded that maternal obesity before pregnancy was associated with increased risks of asthma in their offspring.²⁶ Finally, in the United States, it was found

Table 1

Descriptive and bivariate analysis according to nutritional status in mothers treated at the Peruvian hospitals between 2013-2014 (n=431).

Variables	N	%	Nutritional status of the mother						p
			Normal		Overweight		Obesity		
			N=229	53.1%	N=115	26.7%	N=87	20.2%	
Child sex									0.494
Female	143	33.2	71	49.6	43	30.1	29	20.3	
Male	288	66.8	158	54.9	72	25.0	58	20.1	
Child's age (years)									0.257
2	105	24.4	54	51.4	33	31.4	18	17.2	
3	147	34.1	83	56.5	41	27.9	23	15.6	
4	97	22.5	50	51.6	24	24.7	23	23.7	
5	82	19.0	42	51.2	17	20.7	23	28.1	
Area of residence									0.236
Coast	206	47.8	109	52.9	56	27.2	41	19.9	
Mountains	223	51.7	120	53.8	59	26.5	44	19.7	
Jungle	2	0.5	0	-	0	-	2	100.0	
Gestational age									<0.001
Preterm	45	10.4	12 ()	26.7	31	68.9	2	4.4	
At term	386	89.6	217	56.2	84	21.8	85	22.0	
Birth weight									<0.001
Low	10	2.3	1	10.0	7	70.0	2	20.0	
Insufficient	35	8.1	9	25.7	24	68.6	2	5.7	
Normal	386	89.6	219	56.7	84	21.8	83	21.5	
Prematurity									<0.001
Not	386	89.6	217	56.2	84	21.8	85	22.0	
Yes	45	10.4	12	26.7	31	68.9	2	4.4	
Type of delivery									0.440
Natural	345	80	178	51.6	95	27.5	72	20.9	
Cesarean section	86	20	51	59.3	20	23.3	15	17.4	
APGAR score at 5 minutes after birth									<0.001
Severe depression	5	1.2	0	-	5	100.0	0	-	
Moderate depression	21	4.8	4	19.1	13	61.9	4	19.0	
Normal	405	94	225	55.6	97	23.0	83	20.4	
Silverman and Anderson Test									<0.001
Without respiratory distress	406	94.2	226	55.7	99	24.4	81	19.9	
Mild respiratory distress	20	4.6	3	15.0	11	55.0	6	30.0	
Moderate respiratory distress	3	0.7	0	-	3	100.0	0	-	
Severe respiratory distress	2	0.5	0	-	2	100.0	0	-	
Family history of atopy									<0.001
No	351	81.4	212	60.4	75	21.4	64	18.2	
Yes	80	18.6	17	21.3	40	50.0	23	28.7	
Time of diagnosis of childhood asthma									<0.001

0 to 12 months	0	0	0	-	0	-	0	-
1 to 2 years	0	0	0	-	0	-	0	-
2 to 5 years	90	20.9	10	11.1	43	47.8	37	41.1
Do not have an asthma attack	341	79.1	219	64.2	72	21.1	50	14.7
Number of childhood asthma attacks in the last year								<0.001
0 to 4 attacks	0	0	0	-	0	-	0	-
5 to 9 attacks	52	12.1	8	15.4	26	50.0	18	34.6
10 or more attacks	38	8.8	2	5.3	17	44.7	19	50.0
Did not have any attacks	341	79.1	219	64.2	72	21.1	50	14.7
Age of the mother								0.342
Low tertile (21 to 26)	168	28	98	58.3	36	21.4	34	20.3
Intermediate tertile (27 to 31)	126	29.2	62	49.2	37	29.4	27	21.4
High tertile (32 to 39)	137	31.8	69	50.4	42	30.7	26	18.9
Educational level of the mother								0.023
Primary	14	3.2	8	57.1	5	35.7	1	7.2
Secondary	117	27.2	76	65.0	24	20.5	17	14.5
Higher	300	69.6	145	48.3	86	28.7	69	23.0
History of diabetes mellitus								0.383
Yes	254	58.9	131	51.6	74	29.1	49	19.3
History of high blood pressure								0.983
Yes	187	43.4	100	53.5	50	26.7	37	19.8
History of cardiovascular disease								0.793
Yes	210	48.7	111	52.9	54	25.7	45	21.4
History of respiratory disease during pregnancy								0.195
No	36	8.3	14	38.9	12	33.3	10	27.8
Yes	395	91.7	215	54.4	103	26.1	77	19.5
Consumption of harmful substances								<0.001
Tobacco	9	2.1	8	88.9	0	-	1	11.1
Alcohol	22	5.1	2	9.0	10	45.5	10	45.5
Drugs	4	0.9	1	25.0	3	75.0	0	-
None	396	91.9	218	55.0	102	25.8	76	19.2
Childhood asthma								<0.001
No	341	79.1	219	64.2	72	21.1	50	14.7
Yes	90	20.9	10	11.1	43	47.8	37	41.1

that extremely low or extremely high gestational weight gain in the mother were risk factors for the development of asthma in early childhood due to the long-term impact of intrauterine exposure in children.²⁰

The reasons why overweight and obesity are related to the development of childhood asthma are not fully understood; however, they are believed to be multifactorial and include the relationship between these diseases and respiratory symptoms. In this sense, they are associated with an alteration of lung functional capacity and with

the development of respiratory symptoms, which appear because of a hardening of the airways, a reduction in lung compliance and an increase in alveolar surface tension in the lungs in patients with overweight and especially in those with obesity.¹⁶ The increase in adiposity around the rib cage and abdomen produces an increase in intra-abdominal pressure, which compresses the diaphragm, being considered the equivalent of a chronic abdominal compartment syndrome that gives rise to a decrease in lung volume.¹⁸ Although our study was not designed to assess

Table 2

Descriptive and bivariate analysis according to the incidence of childhood asthma in children treated at the Peruvian hospitals between 2013-2014 (n=431).

Variables	Childhood asthma				p
	No		Yes		
	N=341	79.1%	N=90	20.9%	
Nutritional status of the mother					<0.001
Normal	219	95.6	10	4.4	
Overweight	72	62.6	43	37.4	
Obesity	50	57.5	37	42.5	
Child sex					0.590
Female	116	81.1	27	18.9	
Male	237	82.3	51	17.7	
Child's age (years)					0.356
2	85	80.9	20	19.1	
3	124	84.3	23	15.7	
4	77	79.4	20	20.6	
5	67	81.7	15	18.3	
Area of residence					0.049
Coast	166	80.6	40	19.4	
Mountains	186	83.4	37	16.6	
Jungle	1	50.0	1	50	
Gestational age					<0.001
Preterm	14	31.1	31	68.9	
At term	339	87.8	47	12.2	
Birth weight					<0.001
Low	0	-	10	100	
Insufficient	11 ()	31.4	24	68.6	
Normal	342 ()	88.6	44	11.4	
Prematurity					<0.001
No	339	87.8	47	12.2	
Yes	14	31.1	68	68.9	
Type of delivery					0.241
Natural	281	81.4	64	18.6	
Cesarean section	72	83.7	14	16.3	
APGAR score at 5 minutes after birth					<0.001
Severe depression	0	-	5	100	
Moderate depression	6	28.6	15	71.4	
Normal	347	85.7	58	14.3	
Silverman and Anderson Test					<0.001
Without respiratory distress	348	85.7	58	14.3	
Mild respiratory distress	5	25.0	15	75	
Moderate respiratory distress	0	-	3	100.0	
Severe respiratory distress	0	-	2	100.0	

Family history of atopy					<0.001
No	342	97.4	9	2.6	
Yes	11	13.8	69	86.2	
Time of diagnosis of childhood asthma					<0.001
0 to 12 months	0	-	0	-	
1 to 2 years	0	-	0	-	
2 to 5 years	0	-	90	100.0	
Do not have an asthma attack	341	100.0	0	-	
Number of childhood asthma attacks in the last year					<0.001
0 to 4 attacks	0	-	0	-	
5 to 9 attacks	0	-	52	100.0	
10 or more attacks	0	-	38	100.0	
Did not have any attack	341	100.0	0	-	
Age of the mother					0.688
Low tertile (21 to 26)	135	80.4	33	19.6	
Intermediate tertile (27 to 31)	101	80.2	25	19.8	
High tertile (32 to 39)	105	76.6	32	23.4	
Educational level of the mother					0.101
Primary	10	71.4	4	28.6	
Secondary	100	85.5	17	14.5	
Higher	231	77	69	23	
History of diabetes mellitus					0.623
Yes	203	79.9	51	20.1	
History of high blood pressure					0.991
Yes	148	79.1	39	20.9	
History of cardiovascular disease					0.222
Yes	161	76.7	49	23.3	
History of respiratory disease during pregnancy					<0.001
No	17	47.2	19	52.8	
Yes	324	82.0	71	18.0	
Consumption of harmful substances					<0.001
Tobacco	9	100.0	0	-	
Alcohol	2	9.1	20	90.9	
Drugs	0	-	4	100.0	
None	330	83.3	66	16.7	

Table 3

Crude and adjusted relative risk between the nutritional status of the mother and the incidence of childhood asthma in children treated at the Peruvian hospitals between 2013-2014.

Nutritional status of the mother	Crude			Adjusted		
	cRR	CI95%	p	aRR*	CI95%	p
Normal	Reference	-	-	Reference	-	-
Overweight	8.56	4.46-16.42	<0.001	2.94	1.54-5.60	0.001
Obesity	9.74	5.06-18.73	<0.001	5.10	2.73-9.51	<0.001

* Adjusted for: sex and age of the child, prematurity, type of delivery, family history of atopy, and mother age tertiles.
cRR= crude relative risk; aRR= adjusted relative risk; CI= confidence interval.

differences by sex, it has been reported that the association between obesity and the development of asthma is greater in women than in men.¹⁷ This is due to the role of estrogens, since by increasing the percentage of body fat, the aromatase enzyme present in adipose tissue also increases and is responsible for transforming androgens into estrogens.¹⁹ These hormones have bronchoconstriction action, which worsens the respiratory condition.²⁷

Additionally, increased fatty tissue in people with obesity results in a systemic pro-inflammatory state in which cytokine and chemokine aggregation is increased.²⁸ These inflammatory intermediaries are created and secreted by fat cells and include interleukin IL-6, IL-10, tumor necrosis factor (TNF), C-reactive protein, leptin, and adiponectin.²⁸ TNF is in the cells of fatty tissue and is directly related to the increase of fat in the body, and its concentrations increase in asthmatic pathology and are closely connected with the production of TH2 cytokines (IL-4, IL-6) in the bronchi tissue. Likewise, elevated IL-6 levels in the bloodstream are present in subjects with obesity and are associated with the severity of asthma.²⁸ On the other hand, obese women are more likely to have low levels of vitamin D, which have been associated with an elevated risk of childhood infections and wheezing.²⁹ Likewise, obesity is related to altered microbial colonization, which during pregnancy alters infant intestinal colonization, increasing the later risk of asthma.²⁹

Our results suggest an association that raises the need to prevent overweight and obesity in pregnant women to not only reduce the probability of developing asthma in their children but also prevent other complications associated with these diseases. Overweight or obese mothers are more likely to require an emergency cesarean delivery, develop gestational diabetes, postpartum hemorrhage, preeclampsia, premature rupture of membranes, as well as have a predisposition to surgical site infection.³⁰ On the other hand, newborns born to overweight or obese mothers are at increased risk of neonatal intensive care unit admission, 5-minute APGAR scores less than 7, macrosomia, extreme preterm delivery, fetal congenital anomalies, and perinatal death.³⁰

Our study has some limitations. First, there is a selection bias of the population since we only considered patients of 5 years of age attended in the previously mentioned hospitals. Second, information recorded in medical records was collected, and its quality could not be verified. Third, the diagnosis of childhood asthma is a limitation, since no pulmonary function test such as spirometry was used and the diagnosis was made by the child's clinic, which may have a margin of error. Fourth, we only had permission to access the information of the patients who were treated in hospitals on the coast and in

the mountains, and the jungle would have been a variable of interest to observe the development of the study in the Peruvian state. Lastly, some confounding variables could not be measured due to lack of data, such as prenatal care, medical history of the child, exposure to cigarette smoke or allergens at home, and laboratory tests such as the maternal lipid profile.

In conclusion, being overweight tripled and maternal obesity quintupled the risk of developing asthma in a population of Peruvian children under five years. Weight control measures should be established in pregnant women to prevent the development of asthma and other complications.

Our results reinforce the need to measures to prevent obesity. In this sense, there are recommendations for preconception care of pregnant women with obesity that include receiving information about the risks of weight gain, as well as the benefits of losing weight prior to pregnancy, diet advice and exercises. In, childhood obesity, successful strategies included both parental and family-based interventions in conjunction with modifying the child's diet and physical activity behaviors.

Authors' contribution

Oviedo-Carquín V, Híjar-Zevallos C: Conceptualization, Data curation, Formal analysis, Methodology, Writing-original draft; Urrunaga-Pastor D: Formal analysis, Methodology, Writing-original draft; Herrera-Añazco P: Conceptualization, Methodology, Project administration and Supervision, Writing-original draft, Writing-review & editing. All authors approved the final version of the article and declare no conflict of the interest.

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