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Maternal Obesity as a Risk Factor for the Development of Total Anomalous Pulmonary Venous Connection in Their Offspring

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Summary. The incidence of total anomalous pulmonary venous connection (TAPVC) in the Caucasian population is 2.5/100,000 live births (LB), and the incidence in the Hispanic population is 19.8/100,000 LB. Without knowing the exact etiology for the development of congenital heart disease, our objective was to determine the maternal factors associated with the development of TAPVC.

Methods. 55 mother-child binomials with isolated TAPVC (group I) and 152 healthy mother-child binomials (group II) were included. Both groups had no maternal history of addiction, pre-eclampsia, or type 1, 2 or gestational diabetes mellitus. Complete clinical histories were obtained for the women in both groups and perinatal and birth data were recorded. In addition, genealogies across three generations were constructed to determine affected first- or second-degree relatives with complex congenital heart disease.

Results. Among the maternal characteristics analyzed, women in group I had a higher number of pregnancies before gestation of the index case ($p = <0.05$), and the Body Mass Index (BMI) before pregnancy was higher compared to Group II ($p < 0.05$), with an adjusted risk of OR = 3.6 ($p = 0.011$). The family history showed a higher prevalence in the group of patients with TAPVC compared to healthy children ($p < 0.05$).

Conclusion. Maternal obesity before pregnancy is a risk factor for the development of CATVP in children in the Mexican population.

Key Words: Maternal obesity, Congenital heart disease.

Introduction

Total Anomalous Pulmonary Venous Connection (TAPVC) is defined as a structural alteration in which the pulmonary veins do not connect to the left atrium and instead connect directly to venous systems or drain into the right atrium (1). The international reported prevalence is between 1.5% and 3.6% (1), with a majority of the cases presenting in isolation (68%) (2).

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In contrast to international reports, TAPVC is one of the most frequent complex congenital heart disease (CHD) in Mexico, with an incidence 7.9 fold higher in the Hispanic population than in the Anglo-Saxon population (3). Its etiology and the maternal risk factors associated with its development are not well known (4−10). However, as most cases present sporadically and without association to a particular cause, our objective was to determine whether the presence of pregestational maternal obesity is associated with the development of TAPVC in children.

Materials and Methods

We conducted a retrospective study, prior informed consent was obtained from 55 mother-child pairs (patients with TAPVC) who underwent echocardiographic diagnosis and clinical evaluation to determine an isolated presentation not associated with any extra cardiac of the CHD (Group I). Patients were followed from April 2015−April 2016. A group of 152 healthy mother-child pairs were identified with children born between March 2014 and June 2015 (Group II). Women in this group had a full-term pregnancy (37−40 SDG) with no history of addiction; preeclampsia; or type 1, 2 or gestational diabetes mellitus. Complete medical histories were taken from the women in both groups (I and II), and perinatal and birth data were recorded. In addition, genealogies across three generations were constructed by direct anamnesis to determine whether any first- or second-degree relatives were affected by complex CHD.

Analysis

A comparison of demographic, anthropometric and background data between groups was performed using the Student's t -test for continuous variables and the χ^2 test for categorical variables. The prevalence of overweight and obesity was calculated in each group. To assess the magnitude of the association between the presence of obesity and the development of TAPVC, odds ratios (OR) were calculated using multivariate logistic regression adjusted for maternal age, hereditary family history, number of pregnancies, and sex of the patient. Statistical analysis was performed using STATA/SE 8.0 (STATA Corp., College Station, TX).

Results

Among the characteristics analyzed at birth, patients with TAPVC (group I) showed a higher prevalence of being male, a higher number of weeks of gestation and lower birth weights ($p > 0.05$) (Table 1). Among maternal characteristics, the mothers of children with TAPVC had a higher number of pregnancies before the gestation of the index case ($p = <0.05$) as well as a tendency toward an older age at pregnancy ($p = 0.09$). The Body Mass Index (BMI) before pregnancy was higher compared to mothers in Group II ($p < 0.05$) (Table 1).

The family history of CHD across three generations was higher in the group of patients with TAPVC compared to healthy children ($p < 0.05$) (Table 2).

Women with obesity before pregnancy are more likely to have a child with TAPVC compared to women without obesity (Figure 1), adjusted for the women's age at pregnancy, the number of gestations and the sex of the patients (OR = 3.7; 95% CI 1.5; 9.5).

Table 1. Characteristics at birth of children in groups I and II, and characteristics including maternal age, BMI before pregnancy and number of gestations of women in study groups I and II

Characteristics of children at birth	Group I (n = 55) Media SD		Group II (n = 152) Media SD		p
Sex (♂, n %)	34 61.82		74 48.7		0.033
WG	39.4 ± 1.0		38.7 ± 1.3		0.0005
Size	48.6 ± 4.0		49.1 ± 2.0		0.2313
Weight	2578.8 ± 1114.4		3150.3 ± 379.6		<0.001
Mothers					
Age	25.1 ± 7.3		23.5 ± 5.8		0.0923
Size	1.6 ± 0.1		1.6 ± 0.1		0.8609
Weight	64.2 ± 11.2		59.1 ± 10.9		0.0037
IMC	26.1 ± 4.3		23.9 ± 3.9		0.0006
Number of pregnancies	n	%	n	%	
1	19	34.5	79	52.0	
2	13	23.6	37	24.3	
≥3	23	41.8	36	23.7	0.027

Group I, mothers of patients with TAPVC; Group II, mothers of healthy children; SD, standard deviation; WG, weeks of gestation; BMI, body mass index.

Table 2. Background family history for Congenial Heart Disease and maternal perinatal history of study groups I and II

	Group I		Group II		
	n	%	n	%	p
Family History[a]					
Yes	5	9.09	0	0	<0.001
No	50	90.91	152	100	
Folic Acid Supplementation					
Yes	53	96.36	147	96.71	0.903
No	2	3.64	5	3.29	
Pregestational Folic Acid Supplementation					
Yes	8	14.55	23	15.65	0.258
No	47	85.45	129	84.35	
Alcoholism					
Yes	2	3.64	14	9.33	0.178
No	53	96.36	136	90.67	

[a]Familial history of congenital heart disease: ≥1 first- or second-degree family member affected; MV, multivitamins.