265

Martins K[1], Fonseca A[2], Castro R[1], Girão M[1], Bella Z[1], Silva I[1], Sartori M[1]
1. *Federal University of São Paulo,* ***2.*** *Federal University of Minas Gerais*

COLLAGEN TYPE 3 ALPHA 1 POLYMORPHISM AS A RISK FACTOR FOR GENITAL PROLAPSE

Hypothesis / aims of study
The objective of this study was to verify the possible association between genital prolapse and a polymorphism in the exon 31of the collagen type III-α 1 gene (COL3A1). This polymorphism is caused by a single base substitution from guanine to adenine in the exon 31 COL3A1, resulting in the replacement of alanine with threonine at position 570 of aminoacid sequence of COL3A1.

Study design, materials and methods
A case-control study was conducted in 107 patients with stage III and IV genital prolapse. Control group included 209 women with stage 0 and I prolapse. After extracting genomic DNA from peripheral blood leukocytes, the polymorphism of exon 31 of COL3A1 was typed by restriction fragment length polymorphism.

Results
We did not find differences in the prevalence of GA and AA genotypes between the groups (p = 0.75), even when we grouped patients with at least one polymorphic allele (GA, AA) and compared them with patients without the polymorphic allele (GG) (p = 0.86) (Table 1 and 2). The presence of at least one vaginal delivery (OR 7.22; CI 95% 1.84–28.27), family history for prolapse (OR 2.27; CI 95% 1.04–4.9) and macrosomatic fetus (OR 2.9; CI 95% 1.24–6.79) were independent risk factors for prolapse. Cesarean delivery appeared as a protector factor (OR 0.43; CI 95% 0.24–0.78) (Table 3 and 4)

Interpretation of results
Single nucleotide polymorphisms (SNP) are the most abundant type of DNA sequence variation in the human genome. A SNP is a site on the DNA in which a single base-pair varies from person to person. . The researches want to find a genetic landmark that could predict if a woman has an increase risk for pelvic floor disturbs. As many clinicians are confronted by increased numbers of women requesting elective cesarean deliveries to protect their pelvic floor and perineum, the ability to identify those at risk for POP would be welcome. There is strong evidence that both quantitative and qualitative changes in connective tissue, especially regarding the collagen component, may be responsible for the defective support of the pelvic floor. In our study, we could not identify any association between this polymorphism and genital prolapse. Although the study and control groups were not totally homogenous, the logistic regression model was applied to eliminate the confusing factors and determine the independent risk factors. In our study, we found that age, body mass index, parity, vaginal delivery, forceps delivery, infant birth weight, and positive family history for prolapse were all statistically significantly different in the subjects with severe pelvic organ prolapse compared to subjects with normal support (Table 1). However, multiple logistic regression analysis only identified the presence of at least one vaginal delivery, infant birth weight ≥4,000 g, and family history for prolapse as independent risk factors for prolapse (Table 4). Child birth is believed by many to be the major risk factor for genital prolapse [1, 24], a fact that we were able to confirm with our study. In the study group, 97.5% of the patients had undergone at least one vaginal delivery. Using the logistic regression model, we found that women who had had at least one vaginal delivery were seven times more likely to develop genital prolapse. Cesarean delivery appeared as an important protector factor (OR, 0.43; CI, 0.24–0.78).

Concluding message
Type III collagen exon 31 polymorphism is not a risk factor for genital prolapse.

Table 1: Allele frequencies and genotype distribution on the control and study group

	Control group (n=206)	Study Group (n=107)	χ2	p value
G allele	317 (76,9%)	168 (78,5%)	0,2	0,66
A allele	95 (23,1%)	46 (21,5%)		
GG	125 (60,7%)	66 (61,7%)	0,56	0,75
GA	67 (32,5%)	36 (33,6%)		
AA	14 (6,8%)	05 (4,7%)		

Table 2: Grouped genotype distribution in control and study group

	Control group (n=206)	Study Group (n=107)	χ2	p value
GG	125 (60,7%)	66 (61,7%)	0,03	0,86
GA+AA	31 (39,3%)	41 (38,3%)		

Table 3: Demographic and clinical characteristics of the control and study group

Characteristic	Control group (n=209)	Study Group (n=107)	p value
Mean age (years)	60,86	66,36	<0.0001
Mean body mass index (kg/m2)	26,5	27.8	0,03

Race White Nonwhite	 58,4% 41,6%	 63,6% 36,4%	 0,37
Mean parity (range)	2,01	4,5	<0.0001
Mean vaginal deliveries	1,03	4,01	<0.0001
Mean cesarean deliveries	0,86	0,24	<0.0001
Mean forceps deliveries	0,13	0,25	<0.001
Infant birth weight	3451	3820	0,0002
Mean age at menopause	47,7	48,8	0,15
Positive family history for prolapse	17,2%	28%	0,02
Chronic cough	10,5%	11,2%	0,85
Chronic constipation	31,6%	27,1%	0,41

Table 4: Odds ratio (95% confidence intervals) of the possible independent risk factors for genital prolapse

Variables	p value	OR (95% CI)
One vaginal delivery	0.005	7.22 (1.84–28.27)
Age	0.02	1.05 (1.0–1.1)
Body mass index	0.025	1.08 (1.0–1.1)
Forceps deliveries	0.82	1.06 (0.59–1.9)
Cesarean deliveries	0.006	0.43 (0.24–0.78)
Family history for prolapse	0.038	2.27 (1.04–4.9)
Infant birth weight≥4,000 g	0.014	2.9 (1.24–6.79)

Specify source of funding or grant	**None**
Is this a clinical trial?	**Yes**
Is this study registered in a public clinical trials registry?	**No**
Is this a Randomised Controlled Trial (RCT)?	**No**
What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**São Paulo Federal University Research and Ethics Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**