Int Urogynecol J (2008) 19:1063–1069
DOI 10.1007/s00192-008-0591-1

ORIGINAL ARTICLE

Family history as a risk factor for pelvic organ prolapse

Mary T. McLennan · Jenine K. Harris · Barbara Kariuki · Sara Meyer

Received: 13 December 2007 / Accepted: 14 February 2008 / Published online: 19 March 2008

Abstract The aim of this study was to determine whether a family history of prolapse and/or hernia is a risk factor for prolapse. A cohort of 458 women seeking gynecological care was classified as exposed (family history) or unexposed (without family history). We used χ^2 to assess confounding and logistic regression to determine risk. Nearly half (47.3%) of the 458 participants reported a positive family history. Of these, 52.5% had prolapse. This was significantly higher than the 28.9% rate of prolapse in women without a family history ($p<0.001$). The crude risk ratio for family history of prolapse and/or hernia and prolapse was 1.8 (95% CI 1.4–2.3). After adjusting for vaginal deliveries, incontinence, and hysterectomy, the risk of prolapse was 1.4 (95% CI 1.2–1.8) times higher in women with a family history of prolapse and/or hernia. Heredity is a risk factor for prolapse. History taking should include both male and female family members.

Keywords Family history · Hernia · Prolapse

Presented at Central Association of Obstetricians and Gynecologists Awarded George W. Morley Paper Award Chicago, IL, USA, 17 October 2007

M. T. McLennan (✉) · S. Meyer
Division of Urogynecology,
Department of Obstetrics and Gynecology and Women's Health,
Saint Louis University,
6420 Clayton Rd., Ste. 290,
St. Louis, MO 63117, USA
e-mail: mclennam@slucare1.sluh.edu

J. K. Harris · B. Kariuki
School of Public Health, Saint Louis University,
St. Louis, MO, USA

Introduction

The overall prevalence of prolapse in the US is 21.7% in 18–83 year olds [1], with rates as high as 27% in women 30–49 years old and 30% in women 50–89 years old [2]. The estimated lifetime risk for having a single operation for prolapse or urinary incontinence by age 80 is 11.1% [3]. The National Institute of Child Health and Human Development acknowledges that not enough is known about the causes of prolapse [4]. It is therefore vitally important to understand the natural history and risk factors in order to develop better prevention strategies.

Prolapse is considered a hernia of the pelvic and/or intraperitoneal contents into the vaginal canal. Well-established risk factors include age, parity, and previous hysterectomy, especially if performed for prolapse and collagen disorders [3, 5, 7–9]. Disputed risk factors include body mass, mode of delivery, education, birth weight of infant, race, chronic pulmonary diseases, lifting, and maternal gynecologic history [1, 3, 6–14]. These factors alone may not adequately explain why certain patients develop prolapse. In the Women's Health Initiative, almost one fifth of nulliparous women had some degree of prolapse [15]. Studies have established family history as a risk factor for other pelvic disorders such as urinary incontinence [16]. Could prolapse also have a genetic basis? To date, there is only one study assessing gene expression. Visco and Yuan [17] found there was differential gene expression for the structural proteins in the pubococcygeus muscle between five women with prolapse and five controls. These differences are the result of either genetic mutation or genetic inheritance. There is a small amount of literature noting that patients whose female family members have prolapse are at increased risk

developing of prolapse [17, 18]. In a study of inguinal hernias in women, Liem et al. [19] noted a positive family history as an independent risk factor (OR=4.3, 95% CI 1.9–9.7). Hernias in male or female family members increased the risk. In a prospective study of 8,104 US women with inguinal hernias, Ruhl and Everhart [20] noted a history of a previous umbilical hernia increased the risk of inguinal hernia (HR=3.2; 95% CI 1.2–8.7).

If heredity plays a role in the development of pelvic organ prolapse (POP), it could allow physicians to identify women at high risk and develop early prevention and intervention strategies to decrease the risk and ultimately the prevalence of the disease. Studies to date assessing prolapse risk factors have not included information on male family members or other hernia sites. Our study seeks to establish whether family history of weakened connective tissue as evidenced by hernias in male relatives and by hernias and/or prolapse in female relatives is a significant risk factor for the development of pelvic organ prolapse.

Materials and methods

We conducted a cohort study of nonpregnant women presenting for gynecological care in a university private practice. This study was approved by the Saint Louis University Institutional Review Board in the exempt category. Therefore, women did not have to sign informed consent. The survey was anonymous. Women were selected to participate if they were: (1) presenting to the generalist or urogynecology service at the Saint Louis University Department of Obstetrics and Gynecology, (2) not pregnant, (3) competent to complete a survey, and (4) a new patient (urogynecology service only). Although women presenting to the urogynecology service were only included if they were new patients, they were not excluded if they had previous prolapse. New patients only were used to prevent duplicate completions as patients may have a number of subsequent visits. Excluded were those who were pregnant or seeking oncology consultation, as pregnancy and cancer treatment could affect the risk of prolapse in unique ways and therefore would not provide generalizable information regarding risk factors.

Surveys were distributed between August 2004 and December 2005. While an attempt was made to give the survey to all new patients, some may have been missed as it was distributed by the check-in coordinator. This person however is unaware of the reason for presentation so could not have preferentially given it to any certain patient type. The patients did not know about the survey before arrival and therefore had no opportunity to enquire of the specifics of their family history prior to being seen. Patients have varying degrees of natural interest, but there was no prompted interest on the researchers' part. Using the survey responses, women were classified as exposed or unexposed. The exposed group included women indicating a family history of hernia in male or female family members or pelvic organ prolapse in female family members by responding positively to one or more of the following questions:

1. Has any female in the family had trouble with their bladder, vagina, uterus, or rectum falling out (prolapse)?
2. Has any female in the family had trouble with hernia(s)?
3. Has any male in the family had trouble with hernia(s)?

The unexposed group included women who indicated no family history of genital prolapse or hernia. Women missing exposure status information were excluded from analysis.

The outcome of interest was POP. Women were identified as having POP based on the clinician recording of POP status during a gynecological exam performed at the time of the survey. That is, prolapse status was recorded prospectively not by later review of the chart. Prolapse was classified using the Baden–Walker criteria half-way system [21], with women having any grade of prolapse (1 through 4) being classified as having prolapse. This system was employed for consistency as not all of the generalist physicians were using the pelvic organ prolapse quantification system. The system was explained to the physicians, and all patients were examined on identical gynecological tables in the dorsal lithotomy position while asking the patient to Valsalva. Previously identified potential risk factors such as age, gravity, parity, mode of delivery, incontinence, race, education, body mass index (BMI), smoking, occupation, lifting, chronic cough, hormone therapy, diabetes, prior hysterectomy, and constipation were included as covariates. Information on these covariates was obtained from the questionnaire itself, not by chart review. Women were not specifically asked if they had previous surgery for prolapse, only if they had a hysterectomy and the reason (bleeding, fibroids, falling out, cancer, abnormal pap, other). Lifting has been identified as a risk factor in previous studies; however, it has typically been confined to lifting as a characteristic of a woman's occupation [10]. We included lifting associated with exercise and lifting associated with occupation into a single dichotomous variable (lifting or nonlifting). Exercise status was also included as a covariate.

Statistical analyses were performed using Statistical Package for the Social Sciences (version 13.0) and Statistical Analysis System (SAS; version 9.1) statistical software. For bivariate analyses, we used χ^2 statistics and *t*-tests for independent samples to compare population characteristics between women reporting a family history of prolapse and/or hernia and those reporting no family history. For those characteristics with more than 5% of responses identified as missing or "do not know," a category for unknown was included in the analysis in order

to see if those women with missing information differed significantly in reported history of prolapse and/or hernia.

Following bivariate analyses, we assessed for effect modification and confounding to determine whether (1) the relationship between a family history of prolapse and/or hernia and POP was different at different levels of other variables (effect modification), or (2) the relationship between family history of prolapse and/or hernia and POP was distorted by the influence of one or more other variables (confounding). To assess for effect modification we used the Breslow–Day χ^2 test, which identifies significant differences in the stratum specific estimates of risk. To examine confounding, we calculated the adjusted risk ratio (aRR) and used the 10% rule to identify potential confounders and the Mantel–Haenszel χ^2 test to determine significance.

Using SAS procedure GENMOD, we conducted logistic regression with a binomial distribution and log link function in order to determine the appropriate estimates of the aRR for pelvic organ prolapse given family history of prolapse and/or hernia and any confounders identified. For this analysis, categorical variables were recoded to dichotomous dummy variables.

Results

Six hundred twenty-four women completed the survey during 2004 and 2005. All patients receiving a questionnaire completed at least some of it (no one refused). All patients were from the same office but individual providers were not identified. Of the 624, 477 (76%) included conclusive information regarding family history of prolapse in female family members and/or hernia in female or male family members. This was the initial group for analysis. We did not attempt to contact those 147 women with missing information, as there was no identifying information on the survey. Two hundred and six of the 477 (43%) reported no family history of prolapse or hernia, while 271 (57%) reported at least one family member with this history. There were significant differences in demographic, behavioral, and medical history characteristics between those with a positive family history and those without. Those reporting a family history of prolapse and/or hernia were more likely to be Caucasian, had a higher gravity and parity, had had a hysterectomy, reported incontinence and constipation, and were less likely to exercise. They were also more likely to report a family history of incontinence and hysterectomy (Table 1). The breakdown of conditions reported by the 271 women with a family history is reported in Table 2.

After removing 19 women with missing information from the population, 458 women remained for the subsequent analysis. The 19 women with missing values or "do not know" responses were significantly different from the 458 with complete information. They were more likely to be older, diabetic, and incontinent, diagnosed with prolapse, and fail to report their BMI, family history of hysterectomy, or incontinence.

Analysis of those with complete information, showed that 194/458 (42.4%) were diagnosed with prolapse. Of these, 180 (93.3%) had ≥ grade 2 prolapse. The various grades are as follows: 13 (6.7%) grade 1; 39 (20.2%) grade 2; 68 (35.3%) grade 3; 73 (37.8%) grade 4, with one individual missing grade-level data. Two hundred and sixty-one of the 458 women (57.0%) reported having a family history of prolapse and/or hernia. On initial analysis without considering other variables, the risk for developing prolapse was 1.5 times higher for women with a male relative with a hernia compared to those without family history of male hernia. Similarly, the risk of prolapse was 1.8 times higher for women with a female relative with prolapse and/or hernia compared to women without the female family history of prolapse and/or hernia.

Further analysis of these 261 with a positive family history showed that 137 (52.5%) had the outcome of interest (pelvic organ prolapse), which was significantly higher than the 57 (28.9%) women diagnosed with prolapse of the 197 women who did not have a family history of prolapse and/or hernia ($p<0.001$). The crude risk ratio (cRR) for the relationship between family history of prolapse and/or hernia and pelvic organ prolapse was 1.8 (95% CI 1.4–2.3).

Comparing those with mild prolapse to those with severe prolapse, we found that, of those with severe prolapse (grade 3–4), 110 (78.0%) had a family history of prolapse or hernia and 31 (22.0%) had no family history. Of those with mild prolapse, 27 (50.9%) had a family history, and 26 (49.1%) had no family history. Therefore, the risk of severe prolapse (grade 3–4) was 1.48 (95% CI 1.14–1.90) times higher in those with a family history compared to those without a family history which was statistically significant. In contrast, a positive family history was not a statistically significant risk factor for mild prolapse (grade 1–2) with a relative risk 1.14 (95% CI 0.70–1.87).

Based on a significant Breslow–Day test, we found evidence of effect modification by the number of vaginal deliveries ($\chi^2=7.9$; $p=0.02$). Women with a positive family history and one vaginal delivery had a prolapse rate of 26% compared to 21% in those without a history. With multiple vaginal deliveries, the rate was 76% for those with a family history compared to 48% for those with no family history. However our sample size was not sufficient to further explore this apparent interaction between family history and number of vaginal deliveries. Instead, we included vaginal deliveries as a confounder, which is a biologically plausible alternative.

Table 1 Participant characteristics by family history of prolapse and/or hernia in the 477 women providing conclusive information on family history

	No family history (n=206)		Family history (n=271)		p
	n	%	n	%	
Demographic and behavioral characteristics					
Age (mean, SD)	46.6	17.7	52.8	16.2	0.09
BMI					
≤24.9 (underweight/normal)	86	41.7	104	38.4	0.60
>24.9 (overweight/obese)	112	54.4	159	58.7	
Unknown	8	3.9	8	3.0	
Current exercise	150	73.2	170	63.0	0.02
Education (years)					
≤12	97	47.1	123	45.4	0.67
>12	106	51.5	141	52.0	
Unknown	3	1.5	7	2.6	
Lifting (occupation or exercise)	113	55.7	147	54.9	0.86
Race					
African–American	54	26.2	35	12.9	<0.001
Caucasian	142	68.9	228	84.1	
Unknown–other	10	4.9	8	3.0	
Ever smoker	72	35.1	99	36.5	0.75
Gynecological history					
Cesarean deliveries					
No c-sections	183	89.3	239	88.5	0.84
Single c-section	13	6.3	16	5.9	
Multiple c-sections	9	4.4	15	5.6	
Hysterectomy	58	28.4	114	42.2	0.002
Hormone therapy	75	36.6	93	34.4	0.63
Incontinent	107	51.9	196	72.3	<0.001
Gravidity					
No pregnancies	47	22.8	36	13.3	0.006
Single pregnancy	27	13.1	26	9.6	
Multiple pregnancies	132	64.1	209	77.1	
Parity					
Nulliparous	53	25.7	46	17.0	0.03
Single birth	26	12.6	28	10.3	
Multiple births	127	61.7	197	72.7	
Vaginal deliveries					
None	64	31.1	63	23.2	0.01
Single vaginal delivery	39	18.9	35	12.9	
Multiple vaginal deliveries	103	50.0	173	63.8	
Other medical history					
Chronic cough	15	7.3	21	7.8	0.85
Constipation	48	23.4	93	34.7	0.01
Diabetes	12	5.8	26	9.6	0.13
Family medical history					
Family history hysterectomy					
Yes	78	36.9	149	55.0	<0.001
No	125	60.7	112	41.3	
Unknown	5	2.4	10	3.7	
Family History Incontinence					
Yes	44	21.4	121	44.6	<0.001
No	144	69.9	78	28.8	
Unknown	18	8.7	72	26.6	

Table 2 Breakdown of the types of family history reported by 271 women with a positive history

Type of hernia	Number (%)
Male hernia only	100 (36.9)
Prolapse only	49 (18.1)
Female hernia only	43 (15.9)
Prolapse and male hernia	34 (12.5)
Male and female hernia	17 (6.3)
Prolapse and female hernia	16 (5.9)
Prolapse and male and female hernia	12 (4.4)

We identified confounders by comparing the aRR for each potential confounder to the cRR and identifying differences of 10% or more between the aRR and cRR. Using this 10% rule, we found significant evidence of confounding by number of vaginal deliveries, hysterectomy status, and incontinence. After adjusting for vaginal deliveries, the risk for prolapse was 1.5 (95% CI 1.2–1.9); after adjusting for hysterectomy status, the risk was 1.6 (95% CI 1.3–2.0), and after adjusting for incontinence the risk was 1.6 (95% CI 1.2–2.0) times higher for women with a family history of prolapse and/or hernia compared with women without a family history of prolapse and/or hernia.

Results of the binomial logistic regression with prolapse status as the dependent variable and family history of prolapse and/or hernia, vaginal deliveries, incontinence status, and hysterectomy status as the independent predictors indicated a significant overall result (χ^2=443; $p<$ 0.001; Table 3). The model showed that, after adjusting for these variables, the risk of prolapse was 1.4 (95% CI 1.2–1.8) times higher in women with a positive family history.

Discussion

Given our findings, heredity is a potential risk factor for developing pelvic organ prolapse. This study adjusted for commonly reported risk factors and found the risk of prolapse was 1.4 times higher in those with a family history of prolapse or hernia which was statistically significant. In a review of pelvic organ prolapse, Weber and Richter [22] felt that the pathophysiology was multifactorial and described the "multiple-hit process" whereby genetically susceptible women may be exposed to multiple life events that ultimately result in the development of clinically significant prolapse. Genetically susceptible would imply a potential role for not only the mother's genetic makeup but also the father's. It is in this latter area that we sought additional information by asking specific questions as to whether the father or brothers had a history of hernia, which is considered by most to have a similar pathophysiology to female prolapse. It is the addition of the male family history that makes this study different from others reported to date. A few studies have assessed the role of the female family history. This is the largest to date. Our results are comparable. Jack et al. [18] reported that women whose female family members had prolapse were five times more likely to develop prolapse compared to the general population. On specific analysis of the patients' family tree, they noted that it appeared that there was both maternal and paternal transmission. Buchsbaum et al. [16] evaluated familial risk by comparing the prevalence of prolapse in nulliparous postmenopausal women with the rates in their sisters. They reported a high concordance in the level of pelvic support between the two groups, with some discordance in the level of pelvic support in sister pairs where one sister was parous and the other was not. In a study of Italian women, Chiaffarino et al. [10] reported that the risk of urogenital prolapse was higher in women whose mothers or sisters reported prolapse with an odds ration of 3.2 (95% CI 1.1–7.6).

An interesting question to arise from this study is the effect of the number of vaginal deliveries on the risk of developing prolapse in those who also have a positive family history. We noted that when there was one vaginal delivery the rate of prolapse was similar in those with or without a family history, but with multiple vaginal deliveries the rate of prolapse was 1.6 times higher with a positive family history. We did not have a large enough sample to adequately test this trend statistically; however, it is biologically plausible that the physical damage caused by vaginal delivery triggers or enhances the effect of family history. This alternate model requires further study. We are continuing to recruit patients to enable us to stratify the risk by the number of vaginal deliveries in an attempt to answer this question. Understanding the interaction between the two may be very important in advising young women with affected family members as to the number of vaginal deliveries advisable before risk of prolapse increases significantly. With the increasing trend–demand for elective

Table 3 Association between family history of prolapse and/or hernia, vaginal delivery, and pelvic organ prolapse determined by logistic regression

	Regression coefficient	adjusted Risk Ratio	95% CI
Constant	−2.9		
Family history	0.4	1.4	1.2–1.8
No vaginal deliveries	–	1.0	–
Single vaginal delivery	0.8	2.3	1.1–4.9
Multiple vaginal deliveries	1.8	5.8	3.1–10.7
Incontinence	0.2	1.3	1.0–1.6
Hysterectomy	0.4	1.5	1.2–1.8

Cesarean section, this may play a role in the decision-making process for select patients.

Our study has two main limitations that impact the generalizability of these study results. The patients were recruited from a university private practice. We compared our sample population to the Missouri population for the demographic and behavioral characteristics included in this study. Our subjects were slightly older and more likely to be overweight or obese compared to the general population. However, none of the other demographic or behavioral characteristics were notably different between the two populations. We did not collect income information in our sample but because our location is a private practice, we anticipate that their income would be higher than the general population. There was also a significant difference between women with missing values and those with complete information for our study; however, we did not use any of their information in the analysis and this was a very small number of patients [19].

The second limitation was that we relied on subjects to accurately recall their family history and did not verify their answers. There were a number of women who did not know their family medical history. Once again, women were excluded from analysis if there was any missing information. Patients did not know of the study prior to arriving and therefore were not prompted to know their family history. Therefore, we believe that potential recall bias in our survey responses occurred to the same degree in both our exposed and unexposed patients. This would result in nondifferential misclassification and would bias our calculated relative risk to the null, thus making the true association stronger than our reported value of 1.4. However, we acknowledge those that could argue that women with prolapse may be more likely to ask a family member (differential information bias) or conversely they may be more embarrassed to tell a family member about her organs falling out than she is to tell about heart disease or hypertension. These are not issues that any researcher can control.

In conclusion, while other studies have associated prolapse mainly with age and parity, a family history of prolapse and/or hernia is an additional risk factor that needs to be considered. This study underscores the importance of women knowing their family history (both maternal and paternal) and reporting it to their physician. In addition, researchers should include a history of prolapse or hernia in both male and female family members among the potential risk factors in future studies assessing the pathophysiology of prolapse. Recommendations for counseling based on this information are difficult until further studies are available. However, it would be appropriate to tell a patient that her family history may put her at increased risk and educate her just as we do with patients who do chronic heavy lifting despite limited literature. [6–14]

Acknowledgement Tina Barbaro who as a medical student and Susan Barr MD as a resident aided in the distribution and collection of questionnaires and/or data entry.

Conflicts of interest No conflict of interest for any author.

References

1. Swift S, Woodman P, O'Boyle A et al (2005) Pelvic Organ Support Study (POSST): the distribution, clinical definition, and epidemiologic condition of pelvic organ support defects. Am J Obstet Gynecol 192:795–806
2. Luber KM, Boero S, Choe JY (2001) The demographics of pelvic floor disorders: current observations and future projections. Am J Obstet Gynecol 184:1496–501
3. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL (1997) Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 89:501–506
4. National Institutes of Health (2000) Epidemiologic research on pelvic floor disorders. National Institutes of Health, Bethesda
5. Bump RC, Norton PA (1998) Epidemiology and natural history of pelvic floor dysfunction. Obstet Gynecol Clin of North Am 25: 723–746
6. Fornell E, Wingren G, Kjolhede P (2004) Factors associated with pelvic floor dysfunction with emphasis on urinary and fecal incontinence and genital prolapse: an epidemiologic study. Acta Obstet Gynecol Scand 83:383–389
7. MacLennan AH, Taylor AW, Wilson DH, Wilson D (2000) The prevalence of pelvic floor disorders and their relationship to gender, age, parity and mode of delivery. BJOG 107:1460–1470
8. Tegerstedt G, Miedel A, Maehle-Schmidt M, Nyren O, Hammarstrom M (2006) Obstetric risk factors for symptomatic prolapse: a population-based approach. Am J Obstet Gynecol 194:75–81
9. Jackson SR, Avery NC, Tarlton JF, Eckford SD, Abrams P, Bailey AJ (1996) Changes in metabolism of collagen in genitourinary prolapse. Lancet 347:1658–1661
10. Chiaffarino F, Chatenoud L, Dindelli M et al (1999) Reproductive factors, family history, occupation and risk of urogenital prolapse. Eur J of Obstet Gynecol Reprod Biol 82:63–67
11. Rinne KM, Kirkinen PP (1999) What predisposes young women to genital prolapse? Eur J of Obstet Gynecol Reprod Biol 84:23–25
12. Samuelsson E, Victor A, Tibblin G, Svardsudd K (1999) Signs of genital prolapse in a Swedish population of women 20 to 59 years of age and possible related factors. Am J Obstet Gynecol 180:299–305
13. Swift SE, Pound T, Dias JK (2001) Case-control study of etiologic factors in the development of severe pelvic organ prolapse. Int Urogynecol 12:187–192
14. Progetto Menopausa Italia Study Group (2000) Risk factors for genital prolapse in non-hysterectomized women around menopause. Results from a large cross-sectional study in menopausal clinics in Italy. Eur J of Obstet Gynecol Reprod Biol 93:135–140
15. Hendrix SL, Clark A, Nygaard I, Aragaki A, Barnabei V, McTiernan A (2002) Pelvic organ prolapse in the Women's Health Initiative: gravity and gravidity. Am J Obstet Gynecol 186:1160–1166
16. Buchsbaum GM, Duecy EE, Kerr LA, Huang LS, Guzick DS (2005) Urinary incontinence in nulliparous women and their parous sisters. Obstet Gynecol 106:1253–1258
17. Visco AG, Yuan L (2003) Differential gene expression in pubococcygeus muscle from patients with pelvic organ prolapse. Am J Obstet Gynecol 189:102–112

18. Jack GS, Nikolova G, Vilain E, Raz S, Rodriquez L (2005) Familial transmission of genitovaginal prolapse. Int Urogynecol J 20:1–4
19. Liem MS, van der Graaf Y, Zwart RC, Geurts I, van Vroonhoven TJ (1997) Risk factors for inguinal hernia in women: a case-control study. The Coala Trial Group. Am J Epidemiol 146:721–726
20. Ruhl CE, Everhart JE (2007) Risk factors for inguinal hernia among adults in the US population. Am J Epidemiol 165:1154–1161
21. Baden WF, Walker T (1992) Surgical repair of vaginal defects. JB Lippincott, Philadelphia
22. Weber AM, Richter HE (2005) Pelvic organ prolapse. Obstet Gynecol 106:615–634