Etiological factors for development of pelvic organ prolapse in a rural medical college hospital in north-east Bihar: A retrospective case-control study

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Abstract
Background: Pelvic organ prolapse (POP), including anterior and posterior vaginal prolapse, uterine prolapse, and enterocele, is a common group of clinical conditions affecting millions of women. **Objectives:** The aim of the case-control study was to identify etiological factors predictive for development POP and to determine the relationship between these factors and stage of POP. **Methods:** In a case-control study, 240 patients with primary POP and 308 women without POP were included. Age, parity, smoking, body mass index (BMI), menopause, and hormone replacement therapy (HRT) were investigated. **Result:** Independent risk factors for POP included age over 70, parity higher than 3, and menopause. Age, parity, menopause, and HRT were significantly associated with stage of POP. Genital hiatus (GH) and perineal body (PB) showed a significant positive and negative correlation with age and parity, respectively. Menopause and HRT were also associated with them. **Conclusion:** Age, parity and menopause are possible risk factors of POP and associated with the lengths of GH and PB in POP women. Further, these etiological factors and HRT are significantly correlated with the severity of the disease
Key Words: Pelvic organ prolapse; etiological factor; Stage.

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INTRODUCTION
Pelvic organ prolapse (POP) is a common condition with multifactorial etiology.POP is the descent of intra-pelvic organs such as the uterus, bladder, urethra and rectum due to deficiencies in the pelvic support system. It is a common condition among older women [Fig.1] and the incidence has been reported as high as 39.8%[1]. The lifetime risk of women undergoing surgery for incontinence or prolapse is estimated to be 11% in the USA[2]. The loss of pelvic organ support by dynamic interaction of bony pelvis, endo-pelvic connective tissue and pelvic floor musculature induces POP and the process of disorder development generally occurs over many years. POP is often asymptomatic, but sometimes, it has vaginal bleeding, back or lower abdominal pain, obstructive constipation, heaviness of genitalia and urinary symptoms. There are well-known risk factors for POP, including aging, vaginal birth, birth trauma, chronic increases intra-abdominal pressure (obesity, chronic constipation, chronic coughing, repetitive heavy lifting), menopause, estrogen deficiency, genetic factor, smoking, prior surgery, myopathy and collagen abnormalities[3,4]. Often, a combination of these etiologic factors results in POP. These risk factors vary from subject to subject and can be influenced by race, ethnicity. Also, they may influence the stage or other components of POP (sub-stage, measurement of the genital hiatus, perineal body, and total vaginal length). However, the relationship between these risk factors and the stage or component of POP has not been clearly understood. This study was performed to identify etiological factors predictive for

development POP and to determine the relationship between these factors and stage of POP.
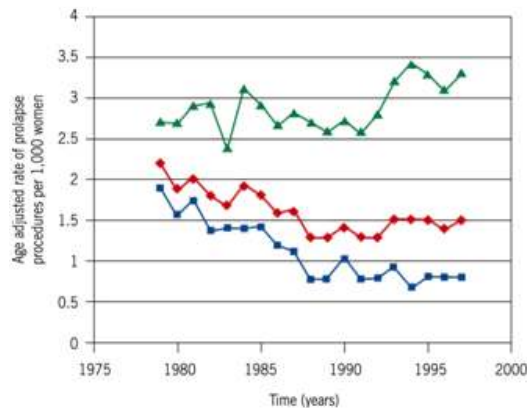
Figure 1: Age-adjusted rates of prolapse procedures per 1,000 women from 1979 to 1997 in the United States, stratified by patient age. Red line, all ages; blue line, women less than 50 years of age; green line, women 50 years or older. Modified from Boyles SH, Weber AM, Meyn L. Procedures for pelvic organ prolapse in the United States, 1979 –1997. Am J ObstetGynecol 2003;188:108 –15. Copyright 2003, with permission from Elsevier.Weber. Pelvic Organ Prolapse. ObstetGynecol 2005

MATERIALS AND METHODS

The study population consisted of 548 patients who visited the gynecology department of the M.G.M Medical College and LSK Hospital, Kishanganj, Bihar, India. Data were collected retrospectively from the *office charts of patients*. All subjects were divided into two groups, 1. POP patient group (defined as POP stage ≥II) and 2. Control group (defined as POP stage 0 or I).Each patient underwent a *standardized uro-gynecologic history* interview and complete physical examination. All patients had pelvic examinations performed both in the supine position and in a 45° upright position in a birthing chair while performing the Valsalva maneuver with maximal effort. Pelvic organ prolapse was quantified according to the International Continence Society's Pelvic Organ Prolapse Quantification (POP-Q) system[5]. Age, parity, smoking, body mass index (BMI), menopause and hormone replacement therapy (HRT) were investigated in all subjects. This study was approved by the Institutional *Review Board.*

Statistical Analysis

Student's t-test was used to compare means for continuous variables and the $\chi2$ test was used to compare categorical data. The Fisher's exact test was performed when the assumptions for the $\chi2$ distribution were violated. Logistic regression analysis was used to identify risk factors that are independently associated with POP. The relationship between risk factors and POP stage or other compartments (sub-stage, measurement of the

genital hiatus, perineal body, and total vaginal length) was estimated with the $\chi2$, Fisher's, ANOVA and Pearson's correlation coefficient tests where appropriate. All tests were performed with SPSS version 20.0 software (SPSS Inc., Chicago, IL, USA) and a p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Analysis of risk factors associated with stage in the POP group

	II (n =59)	III (n =135)	IV (n =46)	P value
Age (years)	53.7±7.51	62.9±8.22[a]	63.9±10.68[a]	<0.001
BMI (kg/m^2)	22.8±2.85	23.9±2.51	22.7±2.97	0.271
Parity	3.3±1.25	3.9±1.68[a]	3.97±1.75[a]	0.005
Menopause				
Yes	40 (67.7%)	120(88.8%)[a]	40 (86.9%)[a]	<0.001
No	19 (32.3%)	15 (11.2%)	6 (13.1%)	
HRT				
Yes	10 (25.0%)	15 (12.5%)[a]	4 (10.0%)[a]	0.001
No	30 (75.0%)	105 (87.5%)	36 (90.0%)	
Smoking				
Yes	5 (8.4%)	8 (5.9%)	3 (6.5%)	NS
No	54 (91.6%)	112 (94.1%)	43(93.5%)	

Data were expressed as mean± SD or as percentages. The same letter indicates insignificant difference between groups based on multiple comparison test. ANOVA test, χ^2 test, Fisher's exact test. p< 0.05.

Table 2: The relationship between categorized risk factors and other measurements in POP

	GH (cm)		PB (cm)		TVL (cm)	
Menopause						
Yes	5.23±1.39	0.001	2.49±0.81	0.001	6.97±0.89	0.417
No	4.25±1.44		3.00±0.96		6.79±1.01	
HRT						
Yes	4.96±1.27	0.136	2.73±0.91	0.017	6.82±0.78	
No	5.27±1.40		2.44±0.78		6.96±0.90	0.48
Smoking						
Yes	5.46±1.67	0.343	2.67±0.87	0.771	6.97±0.84	0.784
No	4.99±1.44		2.56±0.85		6.92±0.91	

Data were expressed as mean±SD or as percentages. GH: genital hiatus, PB: perineal body, TVL: total vaginal length. Student's t-test. p< 0.05

Risk factors for POP: Of the 548 women examined in this study, 240 patients were put in the POP group and

308 patients were included in the control group. Among the evaluated risk factors, the age, parity, and menopause status were significantly different between the two groups (p < 0.001). Multivariate analysis revealed that age over 70 (OR=15.99, 95% CI=1.82–140.78 for ≤49 versus ≥70, p = 0.013), parity values greater than 3 (OR = 5.56, 95% CI=3.29–9.40 for ≤2 versus ≥3, p < 0.001), and menopausal status (OR=7.84, 95% CI=3.75–16.39 for no versus yes, p < 0.001) were the only significant risk factors for POP.

Relationship between risk factors and stage of POP: The overall distribution of POP-Q system stages were as follows: stage II, 24.58% (59/240); stage III, 56.25% (135/240); and stage IV, 19.17% (46/240). According to the disease stages of POP, age (p < 0.001) and parity (p =0.005) increased by a statistically significant level as the disease became more severe. Also, the proportion of women at menopause or not taking HRT increased with advancing stages of POP and these were statistically significant trends (p < 0.001, p =0.001) (Table 1).

The present study population had a relatively higher rate of anterior vaginal prolapse (sub-stage Aa, Ba: 70%) than other sub-stages (Ap, Bp: 5%, C: 25%). When evaluating the relationship between risk factors and the sub-stage of POP, no significant relationship was found.

Relationship between risk factors and other components of POP: In the POP group, the relationship between risk factors and other components such as genital hiatus (GH), perineal body (PB), and total vaginal length (TVL) were examined. The GH length had a significant positive correlation with age (r =0.319, p < 0.001) and parity (r =0.194, p =0.002), whereas PB size showed a significant negative correlation with age (r = −0.25, p <0.001) and parity (r = −0.137, p =0.029). The menopause group showed a significant increase in GH length (p < 0.001) and a decrease in PB size (p =0.001) compared to the pre-menopause group. Notably, the length of PB increased significantly in those who received HRT (p =0.017) (Table 2). However, any significant correlation between TVL and these risk factors was not found.

DISCUSSION

A large proportion of POP patients did not seek medical help in the past, but the number is increasing with the improvement in available medical treatments and increased interest in the quality of life. The International Continence Society defined a system of POP quantification in 1996, which has good intra-observer and inter-observer reliability[5,6]. This POP-Q system contributed substantially to the progress in studying prolapse because it allowed researchers to report findings in a standardized fashion. More recent studies about

prevalence and etiologic factors of POP havebeen reported[7,8]. Weber et al.[9] categorized potential risk factors for POP as predisposing, inciting, promoting, or decompensating events. Furthermore, many investigators uncovered obstetric risk factors for symptomatic prolapse[10,11]. In this study, age over 70, parity values greater than 3, and menopausal status were independent risk factors for symptomatic POP. Hormone therapy, BMI and smoking were not associated with POP. Like these results, Swift et al.[12] reported that it would be difficult to recommend hormone replacement therapy to prevent prolapse. Also, Nygaard et al.[4] noted similarly that POP was not related with conjugated estrogens and medroxyprogesterone treatment when compared with the placebo. This study revealed that age, parity, menopause status, and hormone therapy are related to the stages of POP. When compared to controls, postmenopausal women with POP had reduced total collagen content, decreased collagen solubility, and increased collagen turnover, which all contribute to the development and progress of the POP[13]. The effect of HRT on the treatment of POP or stress urinary incontinence is unclear. Lang et al.[14] reported that serum estradiol and estrogen receptor (ER) levels in uterine ligaments were significantly lower in premenopausal women in the POP group than those in the controls. Therefore, a deficiency in estrogen and ERs may play a role in premenopausal POP. Hormone therapy in postmenopausal women did not decrease the risk of POP, but it was significantly related to the stages of the disease in the present study in that HRT is associated with the progress and severity of the POP. However, there were several limitations in this study. The period between the first round of HRT and menopause, the duration of HRT, or the dose or route of administration were not considered. In this study, the correlation between risk factors with GH, PB and TVL was examined in the POP group. Several studies have focused on hiatus size, perineal body and prolapse. Delancey et al. reported that the size of the urogenital hiatus is larger in women with prolapse compared to the control group and several failed operations were related to the hiatus size[15]. It is known that a widened GH may play a role in the development of POP and is associated with recurrent prolapse[16]. Therefore, weakened levator system by the injury of levator ani muscle and widened GH are responsible for the development of POP. This study not only identified the risk factors of POP, but also evaluated the effect of risk factors on the stage, sub-stage, and component parameters on POP. In conclusion, age, parity and menopause are possible risk factors for the development of POP and they are associated with the lengths of GH and PB in POP women. These risk factors,

along with hormone therapy are significantly correlated with the severity of the disease.

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