Etiological Factors for Pelvic Organ Prolapse and Its Recurrence as a Cause of Stress Urinary Incontinence: An Update Review

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Abstract

Pelvic organ prolapse (POP) and stress urinary incontinence (SUI) are worldwide problems that affect the quality of life of millions of women. Although mortality is rare due to this health issue, it has been shown that self-perception of the body is significantly affected in those with symptoms. SUI and POP share a pathophysiology that is complex in nature. Intrinsic factors including genetics, age, postmenopausal status and ethnicity. Extrinsic factors including parity, history of prior hysterectomy, co-morbidities and employment. Overall, regardless of the initial cause, prolapse often symptomatic is caused by an anatomical flaw in the endopelvic fascial layer. Understanding this different pathophysiology theories is essential for providing effective treatment for these entities. The aim of the present study was to review the etiological factors for POP and its recurrence as a cause of SUI.

Keywords: Pelvic Organ Prolapse; Stress Urinary Incontinence; Etiological factors

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Introduction

The typical pelvic floor has a number of components that keep the pelvic organs in place and prevent pelvic prolapse. In order to avoid prolapse through the genital hiatus, these include the levator ani muscle group, the sacral plexus, and pudendal nerves and connective tissue. The muscle group, which is primarily innervated by the pudenal nerve, serves as the base for the pelvic structures. The proximal, mid-vaginal, and distal ends of the vagina are attached to the connective tissue on three layers by the endopelvic fascia and pelvic viscera **(1)**. The upper two thirds of the vagina are connected to the posterior pelvic wall by the uterosacral ligaments and paracolpium, according to proximal level I suspension. The cardinal ligaments lateral attachments hold the level II or mid-vaginal portion. The third stage shows how the distal vagina is connected to the marginal structures **(2)**.

Female pelvic organ prolapse (POP) has a multifactorial aetiology and is a prevalent condition. Pelvic floor dysfunction is likely caused by interactions between anatomical, physiological, genetic, behavioral, and reproductive variables over the course of a woman's lifetime. From patient to patient, different variables contribute to the development of POP. It is

difficult to unravel the intricate causal chain involving genetic factors, birth defects, connective tissue aging, living choices, and co-morbid factors (3,4).

Women who have symptomatic disorders experience both bodily and mental pain. It significantly harms women's bodily, psychological, and social wellbeing (5). Pelvic floor dysfunction will become more expensive for both the person and the health care system as a whole as the general population ages and has a lower quality of life and lower productivity (6).

In the general female population, there is an 11.1% lifetime chance of undergoing POP surgery. Reoperation rates following POP surgery are reported to be high. Therefore, it appears essential for the best management of women with this condition to identify the risk factors for POP development and its recurrence in order to provide appropriate preoperative counseling, modify patients' expectations, and tailor surgical therapy (7).

Etiological intrinsic factors

1- Genetic:

In vivo measurements of genetic participation have also been made in addition to mouse models. Twin and family populations have been used in the study on this. Analysis of a sample of women with stage 3–4 prolapse who were 44 years old on average showed that family members were five times more likely to experience the condition. These families had a significant penetrance of the dominant type of inheritance (8).

On a population of nulliparous women between the ages of 18 and 24, a twin study was performed to demonstrate the inheritance of bladder neck mobility in comparison to nontwin and dizygotic sisters. Despite the small patient population and consequently low power, the findings showed a 59% genetic variance, supporting a similar finding of positive genetic involvement (2).

2- Collagen matrix

An abnormal collagen matrix foundation that causes POP and SUI is thought to be linked to the failure of normal anatomy. It is well known that people with connective tissue diseases like Ehlers-Danlos syndrome and Marfan syndrome frequently experience urine incontinence and pelvic prolapse. In the early research, SUI was found to be 20% more common in females with Ehlers-Danlos diagnoses than in those without any known connective tissue disorders. It's interesting to note that when these two groups were compared, those with Ehlers-Danlos had a higher incidence of prolapse. It was observed that the Ehlers-Danlos group had a higher parity rate, though the cause of this is unknown (9,10).

Liapis et al. compared paravaginal and uterosacral samples in women with prolapse or stress incontinence to those in healthy women. In comparison to the other groups, there was a notable decrease in type III collagen in the group that had both POP and SUI (11). Other study found a higher frequency of abdominal hernias in women with prolapse provides additional evidence for the function of connective tissue, again highlighting the significance of functional

collagen in the prevention of these disorders **(12)**. Chen et al. came to the conclusion that this deficit is caused by increased degradation of nascent collagen rather than a reduction in collagen production after further examination of endopelvic fascia biopsies from women with incontinence **(13)**.

In a study of Gabriel et al. compared the uterosacral ligaments of individuals with and without prolapse using immunohistochemistry and histology **(14)**. Although there was no change in the amount of collagen type I or smooth muscle between the two groups, the prolapse group had significantly more collagen type III expression (P 0.001). Additionally, prolapse patients' vaginal connective tissue exhibits a greater expression of collagen type III fibres. Decreased collagen synthesis, but this was caused by a rise in the breakdown of nascent collagen **(15)**.

3- Aging:

Age has been identified as an intrinsic component in the development of urinary incontinence and pelvic prolapse in addition to genetics. It is believed that pelvic pain occurs more frequently as people get older. This is thought to be a result of a variety of variables, such as the postmenopausal oestrogen decline and the normal physiologic advancement of the pelvic floor muscles **(2)**. Swift et al. provided evidence to support this hypothesis by demonstrating a rise in the odds ratio for pelvic prolapse for a change in 10 years of age from 1.04 to 1.46 **(16)**.

4- Ethnicity :

A greater incidence of detrusor instability and stress incontinence was seen in the African American population, which was also a predictor of both conditions. Even though these results are significant, the primary variable that this research ignored was the delivery method used in each group, which could have had an impact on the outcomes **(17)**.The distinction between nulliparous women and Caucasians in terms of pelvic floor strength was discovered by the first study to examine Asian women in vivo. Asian women had larger pelvic floor ligaments and fascia, which reduced the likelihood of prolapse occurring frequently **(18)**.

Etiological extrinsic factors

1-Obstetric:

Parity and vaginal delivery were frequently investigated and shown to be risk factors for primary POP **(19-21)**. While in two studies no association between cesarean delivery and primary POP was found **(22,23)**, and two studies found that it was protective when compared with spontaneous or operative vaginal delivery **(24,25)**.

There was a tendency towards an association between higher birth weight and primary POP **(16, 22)**. Glazener et al. found that being older at the time of the first delivery was a risk factor **(25)**. But, another study found no evidence of a significant association **(19)**. With the exception of forceps delivery, which was protective against primary POP when compared with

only spontaneous vaginal delivery, none of the variables of operational vaginal delivery, age at last delivery, or gravidity were significantly associated with each other **(7)**.

Parity and difficult birth were not important risk factors for POP recurrence. On the other hand, parity was a risk factor for main POP. This phenomenon might be caused by the fact that only women with primary POPs are included in studies about POP recurrence, making them a chosen sample of women. Only once was birth weight and age at last delivery examined, and no correlation was discovered **(26,27)**.

2- Hormone replacement therapy:

The urogenital tract contains oestrogen receptors, which suggests that oestrogen may affect the continence system physiologically. Estrogen improves cellular maturation in the bladder, trigone, and urethra and raises urethral blood flow, -adrenergic receptor sensitivity, and urethral closure pressure. These results serve as the foundation for the therapeutic practise of hormone replacement therapy (HRT) for the treatment of incontinence **(28)**.

A cohort study found that using oestrogen and progestin therapy significantly increased the chance of developing incontinence **(29)**. Use of sublingual or transdermal estrogen, as well as use of oestrogen alone or in combination with progestin, carried comparable risks. Hendrix et al. determined that oestrogen alone or oestrogen combined with progestin users had a greater risk of developing urinary incontinence and that HRT should not be used to treat or prevent incontinence using participants in the Women's Health Initiative (WHI) **(30)**.

Incontinence can be enabled by weakened structural support and elevated venous pressure. Similar results are shown at our institution: elastolytic activity was unchanged in the collagen matrix of endopelvic fascia fibroblasts from women with SUI, but was more than five times elevated in the collagen matrix of endopelvic fascia fibroblasts from women without SUI after a one-day exposure to 17-estradiol and remained elevated over the three days of treatment. This is in line with the finding that menopausal HRT puts women of the mainland at an increased risk of incontinence. Differential oestrogen sensitivity and/or reactivity in the local tissue may be indicated by variations in ER expression and elastolytic activity **(31)**.

3- Comorbidity:

Chronic intraabdominal downward pressure may damage the pelvic floor's structural elements. Asthma is a higher risk factor of about 12% due to a chronic cough that is a byproduct of a chronic pulmonary disease **(12)**. A similar effect was replicated in a different study, where the risk of developing urinary incontinence was around 11%.3 In agreement with this, a significant cross-sectional study showed that the prevalence rate among patients who presently smoke increased by 56% **(32)**.

Obesity also seems to impact pelvic floor function. The WHI found patients with a BMI in the range of 25-30 kg/m2 to have 31% of uterine prolapse, 38% of rectocele and 39% of cystocele. These percentages increased with increased BMI values **(33)**. Richter et al intended a

gradual rise of 3% in incontinence with every 1 unit increase in BMI (32). It should be noted, however, that incontinence in this study was measured via a bladder diary versus urodynamics (2).

4- Hysterectomy :

Hysterectomy's impact on POP and urine incontinence has long been studied. A hysterectomy may theoretically harm the pelvic floor if the endopelvic tissue, uterosacral-cardinal ligament supports, and local nerve supply are disrupted. Previous arguments focused on the hysterectomy procedure (vaginal versus abdominal) and the advantages of preserving the cervix in abdominal cases. (i.e., subtotal hysterectomy). Retaining the cervix during hysterectomy avoids damaging the uterosacral and cardinal ligaments, avoiding potential prolapse in the future. However, earlier studies were observational and had a restricted scope due to the use of retrospective data (6, 34).

A trial by Thakar et al compared the outcomes of total hysterectomy and subtotal hysterectomy with a one-year follow-up. The preoperative and postoperative rates of urinary frequency, stress incontinence, urgency, poor stream and incomplete bladder emptying did not differ significantly between the two groups. Urodynamic studies showed a reduction in stress incontinence after surgery in both groups (35).

A study of short-term outcomes, including hospital stay, time spent getting back to normal activities, and the number of febrile episodes, revealed that vaginal hysterectomy had more overall advantages than abdominal hysterectomy (36).

5- Occupation :

Although there is little information on the impact of employment on POP and stress incontinence, the studies that are available seem to support the notion that occupation has an effect on pelvic functionality (37). A preliminary study found that jobs involving heavy lifting may be a risk factor for prolapse, as evidenced by the higher rate of prolapse surgeries in this population. In a study by Chiaffarino et al. found that housewives had a significantly higher risk of prolapse than did women in managerial roles, presumably because they do more physical work (38).

To further stratify different occupations with their concurrent risks of prolapse, Woodman et al found the greatest odds ratio of 7.75 in factory workers and laborers. This was followed subsequently by housewives, service workers, technical workers and professionals (39).

Conclusion:

POP and SUI are common health issues that affect women globally. Many factors that contribute to the development of POP and SUI such as collagen integrity, genetics and ethnicity, age, parity, occupation and co-morbid health issues.

POP has a strong etiological link to the first vaginal birth. Forceps delivery is the primary modifiable risk factor for POP and should be avoided whenever possible.

Certainly, when evaluating and diagnosing patients, an understanding of the aetiology is crucial.

There is a clear need for long-term, large-scale, prospective research in the area of the pathophysiology of these conditions in order to find novel treatments and concentrate on the preventative factors, despite the fact that there is significant data currently available.

Conflict of interest: The authors declare no conflict of interest.

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