

Pelvic Organ Prolapse in Young Balinese Women: A Case Series

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ABSTRACT

Introduction: Pelvic organ prolapse (POP) is an important health problem but it is still receiving little attention, patients often seek medical help only when the disease is very disturbing/severe.

Case description: This case report describes a series of three cases of POP in a young woman who had similar profiles in terms of several characteristics, including age, occupation, ethnicity, BMI, parity, age of the youngest child (years), number of vaginal deliveries, operative vaginal deliveries, episiotomy, birth weight of the largest child, family history of prolapse, diagnosis, and procedures performed. In this case series, conservative operative treatment (purandare hysteropexy) was carried out, then an examination of the sacrouterine ligament tissue was performed from the operation. The results of the examination showed a decrease in the expression of type I collagen, an increase in type III collagen, an increase in the levels of matrix metalloproteinases-2 (MMP-2), and MMP-9 which based on previous studies are found in patients with POP.

Conclusion: Conservative treatment with purandare hysteropexy were done in all case, further research is needed to establish whether this condition is the cause of the occurrence of POP in young people and the genetic correlation associated with the disorder.

Keywords: Ligament, Pelvic, Prolapse, Treatment.

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INTRODUCTION

Pelvic organ prolapse (POP) is the descent of one or more pelvic organs (bladder, uterus, and rectum) from the anterior vaginal wall, posterior vaginal wall, uterus (cervix) or vaginal apex (vaginal stump after hysterectomy). Pelvic organ prolapse can worsen the quality of life because it can cause abnormalities in the bladder, digestive tract and sexual function disorders, which indirectly cause psychosocial stress and emotional disturbances in the form of depression, isolation and anxiety.^{1,2}

Increasing age, parity, obesity, operative vaginal delivery, large infant weight, and conditions that cause increased intra-abdominal pressure are generally believed to be risk factors for POP, given the high incidence of POP in this population. However, with the discovery of cases of POP at a young age and low parity even in nulliparous patients, other factors in the occurrence of POP have also begun to be investigated, including the role of genetic factors and abnormalities in collagen metabolism. Pelvic organ prolapse management is carried out conservatively or with surgery, both conservatively and radically.³

CASE DESCRIPTION

Patient 1

A 34-year-old Balinese woman came with a complaint of a lump coming out of the birth canal (vagina) since 4 years ago after giving birth to her last child, and has been getting worse since the last 2 months. There was no urinary or defecation complaints. The patient gave birth twice, the first child was born vaginally weighted 3,000 gms 7 years ago and the second child was born by cesarean section weighted 2,800 gms 4 years ago. The patient had a history of episiotomy. The patient used IUD for 2 years with no family history of uterine prolapse. The patient's body mass index was 21.77. The patient was diagnosed with stage III uterine

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prolapse, stage III cystocele, and stage II rectocele. The patient was discharged 2 days after surgery with no complaints. From the last follow-up, patient did not feel any recurrence of complaints until 2 years after surgery (Table 1).

Patient 2

A 35-year-old Balinese woman came with complaints of a lump coming out of her vagina since 2 weeks ago. Patient also complained of pain in the lower abdomen and difficulty during sexual intercourse. The patient gave birth vaginally twice, the first child was born 8 years ago weighted 2,700 gms and the second child 7 years ago weighted 3,000 grams. The patient had a history of episiotomy. The patient did not have a history of previous surgery. She had history of asthma since childhood. There was no family history of uterine prolapse. Patient was diagnosed with grade III uterine prolapse, grade III cystocele, and grade III rectocele. She was discharged 2 days after surgery with no complaints. From the last follow-up, the patient did not feel any recurrence of complaints until 2 years after surgery (Table 1).

Table 1: Characteristics of patients

Characteristic	Patient 1	Patient 2	Patient 3
Age	33	34	34
Job	Employee	Employee	Construction workers
Ethnicity	Balinese	Balinese	Balinese
BMI	Normal	Normal	Normal
Parity	2	2	0
Youngest child (years old)	4	7	0
Number of vaginal deliveries	1	2	0
Operative vaginal delivery	No	No	No
Episiotomy	Yes	Yes	–
Largest birth weight	3,000 gm	3,000 gm	–
Family history of prolapse	No	No	No
Diagnosis	Stage III uterine prolapse, stage III cystocele, grade II rectocele	Stage III uterine prolapse, stage III cystocele, stage III rectocele	Stage IV uterine prolapse, stage III cystocele, stage II rectocele
Treatment	Hysteropexy purandare, anterior colporrhaphy, kolpoperineuraphy	Hysteropexy purandare, anterior colporrhaphy, kolpoperineuraphy	Hysteropexy purandare, anterior colporrhaphy, kolpoperineuraphy
Collagen I expression	Decrease	Decrease	Decrease
Collagen III expression	Increase	Increase	Increase
MMP 2 expression	Increase	Increase	Increase
MMP 9 expression	Increase	Increase	Increase

Patient 3

The third patient is a 34-year-old Balinese woman. The patient came with the complaint of a lump coming out of the birth canal since 1 year ago. The patient's occupation for the last 5 years is a construction worker who lifts bricks every day. The patient has never been pregnant. There is no family history of POP. The patient's body mass index was normal. The patient was diagnosed with grade IV uterine prolapse, grade III cystocele, and grade II rectocele. Patient was discharged 3 days after surgery with no complaints. From the last follow-up, patient did not feel any recurrence of complains until 2 years after surgery. She has not been pregnant ever since (Table 1).

Collagen Type I, Collagen Type III, MMP-2, and MMP-9 Expression

All staining of sacrouterine ligament were done using immunohistochemistry method (IHC). All patients in this case series had decreased expression of type I collagen in their sacrouterine ligaments (Fig. 1). All patients in this case series showed increased expression of type III collagen in the sacrouterine ligament preparations (Fig. 2). Matrix metalloproteinases-2 (MMP-2) expression was increased in all patients in this case series (Fig. 3). All patients in this case series had increased MMP-9 expression in their sacrouterine ligament preparations (Fig. 4).

DISCUSSION

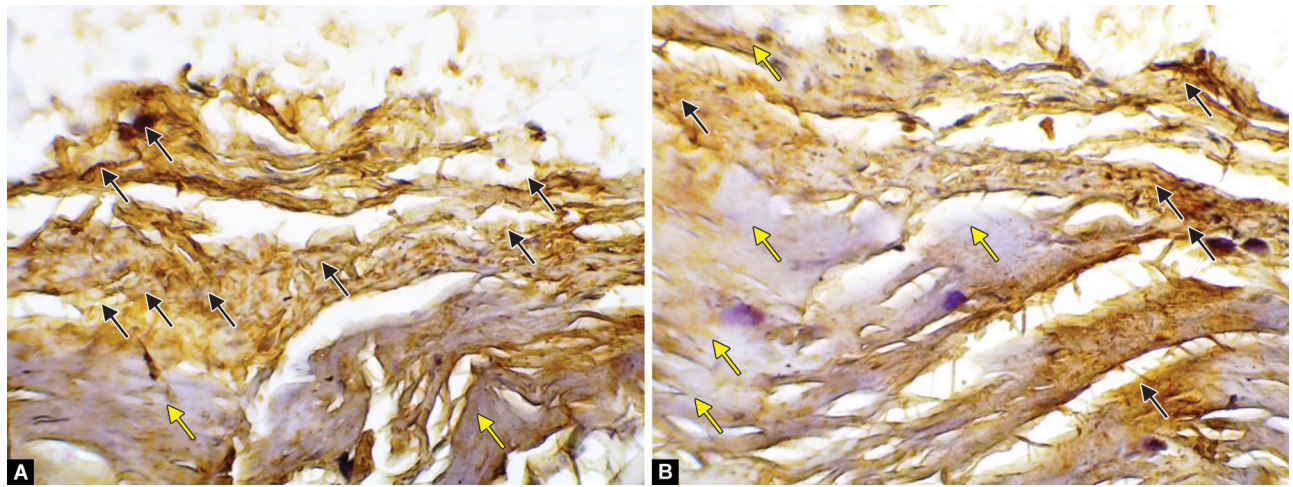
The patients in this case series were aged 33–34 years and had not yet experienced menopause. This age is considered young for patients with POP, which mostly occur to postmenopausal women and peaked after sixth decades of life. Two of the patients in this case series do not often lift heavy loads during work. Conditions that cause repeated increases in intra-abdominal pressure are

widely believed to be a risk factor for the occurrence of POP.⁴ All three patients in this case series had normal BMIs. Women who are overweight and obese have an increased risk of POP. The risk of POP increases with increasing parity.⁵ Study showed that more than half of relatively young premenopausal primiparous women had some form of clinically significant POP 1–4 years after delivery of their first child. According to studies of women younger than 50 years of age, the risk of stress incontinence is increased after forceps delivery compared with spontaneous one.

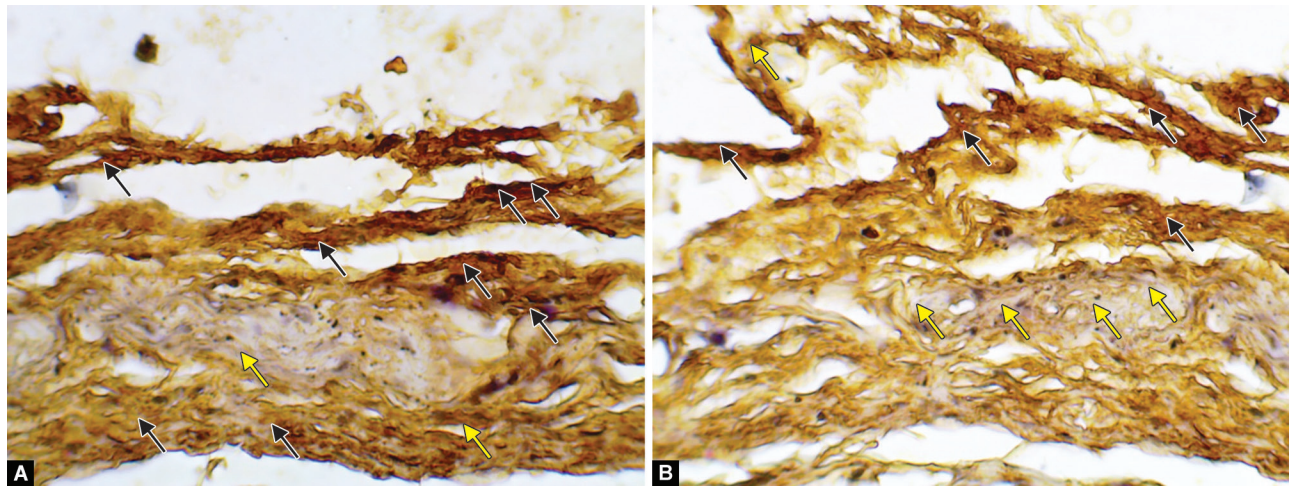
All patients in this case series gave birth to children with a birth weight of 3,000 gm or less. Increased infant weight at birth appears to be associated with an increased risk of POP. Survey of women who had given birth once 20 years previously ($n = 5236$) found that symptomatic POP increased 3% (odds ratio 1.03, 95% CI: 1.02–1.05) for every 100 gm increase in birth weight of the baby. All patients in this case series had no family history of POP.

The results of recent years have shown a high prevalence of POP in Balinese women. Balinese women are believed to be more at risk of experiencing health problems due to hard work (lifting heavy weight during working), giving birth repeatedly due to custom of having at least four children, gene polymorphism of COL1A1, LOXL-1, MMP-9, MMP-2, MMP-9, the presence of genetic variations such as polymorphisms in the estrogen receptor gene and COL3A1 increased the risk of POP by 5.5 times and 3.25 times, respectively. In a 2013 study, the diameters of the transverse and intertuberous pelvic bones of Balinese women who suffered from POP were wider than those who did not experience POP.^{6–8}

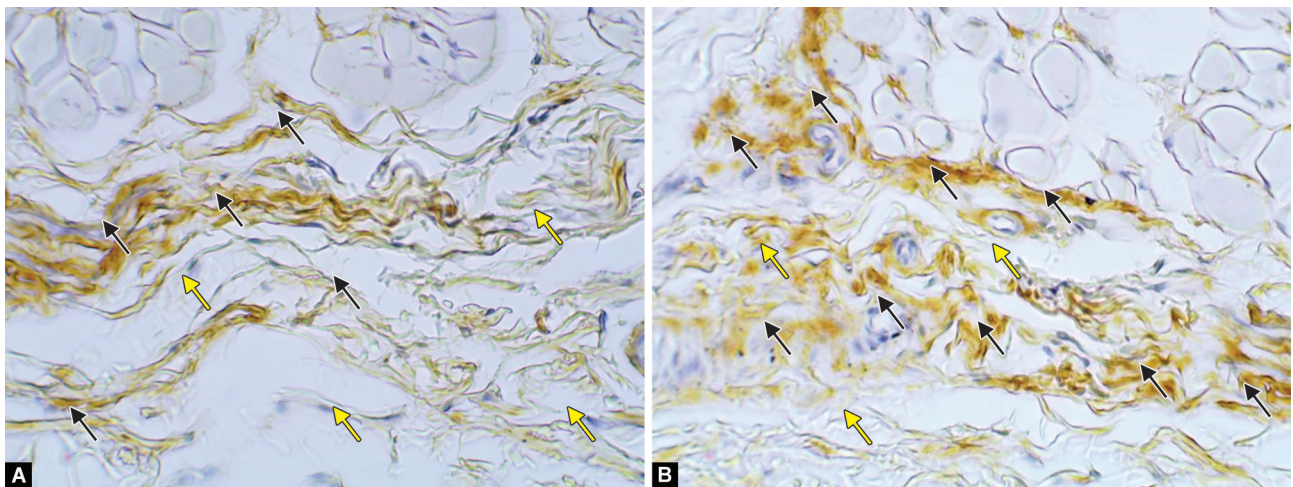
The diagnosis of patients in this case series was classified as severe, namely, uterine prolapse grade II–III, all had grade III cystocele, and grade II–IV rectocele. Many women with prolapse come when the disease has reached a severe degree because they tend to ignore the initial appearance of symptoms and get to the point where



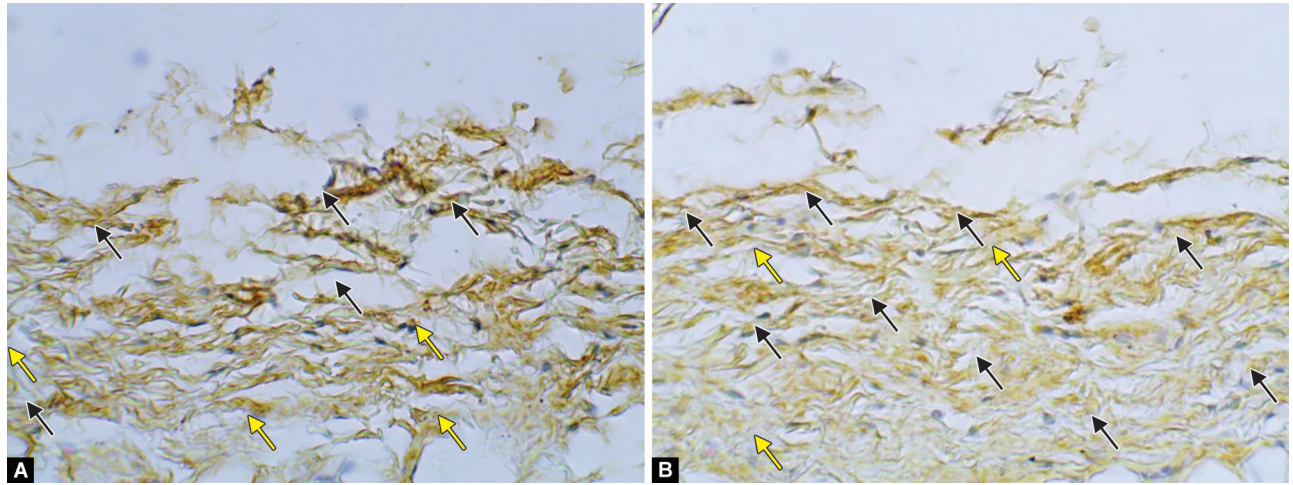
Figs 1A and B: Collagen expression with type I collagen IHC staining. (A) Group of normal ligaments. Expression of type I collagen with brown collagen fibers appeared wider and thicker. Black arrows indicate intact collagen fibers; (B) Group of prolapsed ligaments. Yellow arrows represent type I collagen expression with brown collagen fibers appearing thinner



Figs 2A and B: Collagen expression by IHC Collagen type III staining. (A) Group of normal ligaments. Black arrows indicate intact collagen fibers. Yellow arrows indicate type III collagen expression with brown collagen fibers appearing thinner; (B) Group of prolapsed ligaments. Collagen expression with brown collagen fibers appeared wider and thicker indicating an increase in type III collagen



Figs 3A and B: Collagen expression by IHC MMP-2 staining. (A) Group of normal ligaments. MMP-2 expression is brown; (B) Group of prolapsed ligaments. The black arrow shows the expression of MMP-2



Figs 4A and B: Collagen expression by IHC MMP-9 staining. (A) Group of normal ligaments. Brown MMP-9 expression appears less. The yellow indicates the absence of MMP-9 expression; (B) Group of prolapsed ligaments. Black arrows indicate increased MMP-9 expression

the prolapse is out of the vagina (grade III). Measurement of the degree of prolapse that requires a pelvic exam is also increasingly making women reluctant to get themselves checked properly. Measurement of symptomatic prolapse is more clinically relevant, because asymptomatic prolapse does not require treatment. Even this is a research challenge because prolapse symptoms may take longer to develop than incontinence symptoms and symptoms (e.g., vaginal bulge or pressure, urinary retention, difficulty passing a bowel movement) are less specific. Thus, even symptomatic prolapse cannot be well quantified with symptom questionnaires.⁹ Furthermore, the use of surgery as a surrogate measure for prolapse prevalence did not detect the number of women with symptomatic prolapse who had not undergone surgical treatment. All patients in this case series underwent purandare hysteropexy, anterior colporrhaphy, and colpoperineuraphy.

All patients in this case series had decreased expression of type I collagen in their sacrouterine ligaments. Several studies have shown that connective tissue abnormalities and remodeling are factors that influence the occurrence of POP. All patients in this case series showed an increase in type III collagen expression. The results of this study are consistent with previous findings, showing a statistically significant increase in type III collagen synthesis in participants with a prolapsed uterus. However, this study found no statistically significant association with cystocele or rectocele.²

Matrix metalloproteinases-2 expression was increased in all patients in this case series. MMPs are major regulators of connective tissue degradation and are therefore involved in tissue remodeling. The activity of the enzymes MMP-2 and MMP-9 is higher in urogenital prolapsed tissue than in normal tissue, gelatinase may play a role in collagen degradation in POP.¹⁰ Elastin plays an important role in providing pelvic organ support as shown in elastinopathy models, and women with abnormalities Genetics on elastin metabolism, such as cutis laxa, have an increased risk of developing POP.

In all patients in this case series, there was an increase in the expression of MMP-9 in their sacrouterine ligament preparations. Both immature and mature elastin and the elastin-degrading enzyme MMP-9 are elevated in the vagina of women with POP. This is directly proportional to the number of active MMP-2 which increases. Interestingly, although tropoelastin and desmosine

behave independently of each other in the prolapsed vagina, the highest levels of both proteins occur in postmenopausal women rather than on hormone therapy.

CONCLUSION

In this case series, conservative treatment was carried out, namely, Purandare hysteropexy, then an examination of the sacrouterine ligament tissue was performed from the operation. The results of the examination showed a decrease in the expression of type I collagen, an increase in type III collagen, an increase in the levels of MMP-2, and MMP-9 which based on previous studies proved to be common in patients with POP. Further research is needed to establish whether this condition is the cause of the occurrence of POP in young people and the genetic correlation associated with the disorder.

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