Understanding clinical features of adenomyosis: a case control study

A Shrestha and LB Sedai

Department of Obstetrics and Gynecology, Chitwan Medical College Teaching Hospital, Bharatpur, Nepal

Corresponding author: Dr. Anju Shrestha, M.D., Lecturer, Department of Obstetrics and Gynaecology, Chitwan Medical College Teaching Hospital, Bharatpur, Nepal; e-mail: anjushr2002@yahoo.co.in

ABSTRACT

Adenomyosis is largely under diagnosed before hysterectomy and commonly co-exists with uterine fibroid. Thus this study aimed to elicit the clinical profile of adenomyosis by comparison with uterine fibroid. This is a hospital based prospective case-control study carried out from 1st April 2010 to 31stMay2011which comprise of women undergoing hysterectomy with a histological diagnosis of sole adenomyosis without fibroid , women with both adenomyosis and fibroid and women with fibroid but no adenomyosis. Ambulatory records were performed. The study comprised 150 women, 78(52%) women with adenomyosis without fibroid, 27(18%) women with both adenomyosis and fibroid, 45(30%) women with fibroid but no adenomyosis. Among women with adenomyosis alone,78.2% had menorrhagia,73.1% had dysmenorrhoea,76.9% had chronic pelvic pain and women with adenomyosis and fibroid had menorrhagia in85.2%, dysmenorrhoea in51.9%, chronic pelvic pain in48.1% compared with women of fibroid alone had menorrhagia in75.6%,dysmenorrhoea in 66.77%, chronic pelvic pain in51.1%. Women with adenomyosis group had significantly more of chronic pelvic pain (p-value: 0.003) and had significantly greater parity (p-value: 0.002). Size of uterus was significantly smaller in adenomyosis group (p-value: 0.018) as well as significantly more tender uterus was found in adenomyosis group (p-value: 0.000). Adenomyosis is more frequent among women reporting dysmenorrhoea, menometrorrhagia, chronic pelvic pain and along with bulky uterus. Women with fibroid alone has more of menorrhagia than pain and is associated with enlarge uterus. If women have small fibroid uterus but have more symptoms – think about co-existence of "ADENOMYOSIS".

Keywords: Adenomyosis, fibroid, hysterectomy.

INTROUCTION:

Name Adenomyosis synonyms endometriosis interna, uterine endometriosis, internal endometriosis. By definition, adenomyosis consists of endometrial glands and stroma ectopically placed in the myometrium, at least one high- power field from the base of the endometrium. Leiomyoma (fibroid or myomas) are benign uterine smooth muscle tumors.[1]

Both uterine leiomyomas and adenomyosis are important clinical problems in gynecology, often resulting in hysterectomy for premenopausal women. Both adenomyosis and leiomyomas commonly coexist: concomitant adenomyosis in hysterectomy specimens of women with fibroid ranges from 15- 57%.[2-7] when concomitant adenomyosis is present the risk of treatment failure i.e. – uterine artery embolization (UAE) and magnetic resonance –guided focused ultrasound (MRgFUS); seems to be increased for both methods. [8,9] Studies in vitro suggest that leiomyoma and adenomyosis may share some common pathogenetic mechanisms. Specific cytogenetic rearrangements including deletion of chromosome 7q and dysregulation of the fibroblast growth factor (FGF) system have been reported in both conditions.[10-12]

Little is understood regarding the pathogenesis and clinical features of adenomyosis. Chronic pelvic pain, abnormal heavy uterine bleeding, dysmenorrhoea are symptoms thought to be suggestive of and attributable to the presence of adenomyosis in clinical observation.[13-15]

Given the limitation of USG in diagnosing adenomyosis, and gynecologists reliance on USG findings, adenomyosis is often undiagnosed before hysterectomy and so contribution this disease to the symptoms is only understood retrospectively.[7]

The current study aim is to elicit the clinical profile of adenomyosis by comparison with uterine fibroid. By identifying adenomyosis in women with leiomyoma will allow improved clinical decision making and plan of treatment.

MATERIALS METHODS

This is a hospital based prospective study carried out in chitwan medical college teaching hospital from 1st April 2010 to 31stMay2011. This study comprised women who had undergone abdominal, vaginal or laparoscopic hysterectomy with histopathologically proven adenomyosis and /or fibroid. Comparison was

Table-1: Characteristics of the study population (n=150)

Variable	Adenomyosis (n=78)	Adeno+fibroid (n=27)	Fibroid alone (n=45)	p- value
Age in yrs (mean±SD)	45.8±8.3	46.03±5.3	43.6±6.8	0.25[a]
Parity (Median/Range)	3.5(0-8)	3(1-9)	3(0-7)	0.02[b]
Hb in gm% (mean±SD)	10.3±1.5	10.11±2.2	10.3±1.6	0.82[a]
Duration of symp in yrs (median/range)	3(1-9)	2.5(1-12)	3(1-15)	0.9[a]

[a]One way ANOVA test, [b]kruskal-wallis

done between women of adenomyosis without fibroid with women with both adenomyosis and fibroid and women with fibroid but no adenomyosis. Ambulatory data was collected before hysterectomy in clinically suspected cases of fibroid and adenomyosis and after histopathological report in those where clinical diagnosis of fibroid and adenomyosis was not made. Data were collected on age at surgery, parity, clinical signs and symptoms, pre-op Hb, menopausal status, as well as gross and histopathological findings. Other histopatjhological variables – endometrial status and cervical findings were also noted.

Adenomyosis was diagnosed when the distance between the lower border of the endometrium and the affected myometrial area was over one- half of a low power field (i.e. 2.5mm).

Statistical analysis: The data were analyzed with Epi-Info and SPSSl software. Quantitative variables were summarized by means and S.D variables, following non- normal distribution were summarized by median and range. Mean values were compared using one way ANOVA and kruskal-wallis. Categorical variables were summarized by frequencies (%) and were compared using Pearson chi- Sq. test or fisher exact test.

RESULTS

A total of 150 Women were included in this study. Out of which78 (52%) women had adenomyosis alone, 45 (30%) had fibroid alone and 27 (18%) Women had both adenomyosis and fibroid. General characteristic of study population were summarized in Table-1 where mean age, pre-op Hb level and mean duration of symptoms were similar in three groups. However women with adenomyosis had significantly greater parity compared to fibroid (p- value: 0.002).

Clinical symptoms of women are summarized in Table-2, where more of heavy Uterine bleeding, chronic pelvic pain and dysmenorrhoea were found in all three groups but women with adenomyosis group had significantly more of chronic pelvic pain (p-value:0.003).

Per vaginal examination findings were elaborated on Table-3 where size of uterus is significantly smaller in adenomyosis group (p-value: 0.018) as well as significantly more tender uterus found in adenomyosis group (p-value: 0.000). 75.7%of women with adenomyosis had either normal or bulky uterus but 40% of women with fibroid had more than 10 weeks size uterus. Volume of uterus was calculated by measuring length, breadth and thickness of hysterectomies uterus, which shows that adenomyosis group had significantly lesser volume of uterus :< 150 cm3.

Comparison between adenomyosis group with fibroid group and adenomyosis group with adenomyosis and fibroid group were done. Significant findings we found were shown in Table-4.

Types of endometrium in histopathological examination of study population are shown in Fig. 1. Women with adenomyosis had more of proliferative type of endometrium (38.5%), however 31.1. % women with fibroid had endometrial hyperplasia either simple with or without

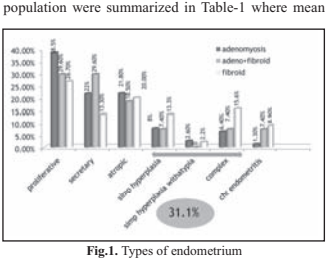

Fig.1. Types of endometrium

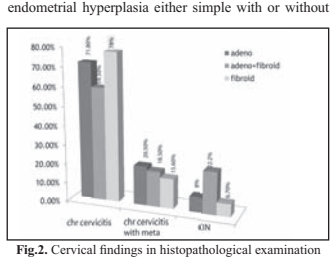

Fig.2. Cervical findings in histopathological examination

Table-2: Clinical symptoms of patients

Symptoms	Adenomyosis (N=78),n(%)	Adeno+ fibroid (N=27),n(%)	Fibroid (N=45),n(%)	p-value
Heavy uterine bleeding	61(78.2%)	23(85.2%)	34(75.6%)	0.621 a
Chronic pelvic pain	60(76.9%)	13(48.1%)	23(51.1%)	0.003 a
Dysmenorrhoea	57(73.1%)	14(51.9%)	30(66.7%)	0.127 a
Dyspareunia	19(24.4%)	6(22.2%)	10(22.2%)	0.953 a
Painful bowel movement	6(7.7%)	2(7.4%)	5(11.1%)	0.8 b
Pelvic pressure	8(29.6%)	8(29.6%)	22(48.9%)	0.274 a

[a]pearson chi-squared test, [a]Fisher exact test

hyperplasia or complex hyperplasia without atypia.

Histopathological examination of cer vix was shown in Fig. 2 where maximum no. of women had chronic cervicitis in all three groups. However 22.2% of women with adenomyosis and fibroid group had CIN 1 or CIN 2.

DISCUSSION

Our study shows that there are many different features in women with adenomyosis alone when compare to women with fibroid and adenomyosis or fibroid alone. The mean age of hysterectomy in the present adenomyosis group was 47 years, which is consistent with most studies done before.[16]

Adenomyosis was rarely diagnosed correctly preoperatively and still largely under diagnosed as it has no special symptoms of its own. Chronic pelvic pain, dysmenorrhoea and abnormal heavy uterine bleeding with irregular menstrual cycle are most frequent symptoms found in our study related with adenomyosis. In contrast we found women with fibroid alone had more of menorrhagia with regular cycle and less of chronic pelvic pain and dysmenorrhoea. Hence there is significantly more frequent chronic pelvic pain and menometrorrhagia with adenomyosis than fibroid. Consisted finding were reported in literature also where only 20% -25% of the women with fibroid had chronic pelvic pain.[17-19]

Exact pathogenesis of adenomyosis is not known , however improper uterine contraction during menses, increased endometrial surface, over production of prostaglandin, and hyperestrogenism are listed as causes of menorrhagia, where as dysmenorrhoea might be caused by uterine irritability or pseudodecidual edema around the adenomyosis foci.[20,21]

Women with adenomyosis in the present study had significantly greater parity than women with fibroid. Moliter and Azziz studies also reported that multiparty has been associated with an increase frequency of adenomyosis.[20,22] Some authors have rendered the opinion that the stresses of labor and delivery and subsequent uterine repair allow the lining cells to invade the muscle wall. However adenomyosis can also occur in women who have never been pregnant. Finally, epidemiologic evidence indicates a decreased risk of fibroid for parous women compared with nulliparous women due to hormonal and non – hormonal mechanisms.[23-25]

Clinical series have suggested that the frequency of the adenomyosis increases with age until menopause and level off thereafter.[22] In concord with earlier studies, we also found less no of adenomyosis in menopausal women. But when compared to women with fibroid significantly more number of menopausal women was found with adenomyosis. This may be the fact that fibroid is estrogen dependent which

Table-3: Size of uterus and tenderness

Uterine size	Adenomyosis (n=78)	Adeno+fibroid (n=27)	Fibroid (n=45)	p-value
Clin. Examination				
Normal	23(29.5%)	2(7.4%)	6 (13.3%)	
Enlarge	55(70.5%)	25(92.6%)	39 (86.7%)	0.018 [a]
Tender uterus	30(44.1%)	5(18.5%)	4 (8.9%)	0.000 [b]
Vol. of uterus cm3 (median/range)	109(14-510)	232 (48-960)	265 (38-1584)	1.00 [c]
<150cm3	56(71.8%)	8 (30.8%)	14 (31.8%)	0.000 [a]
150-400cm3	21(26.9%)	12 (46.2%)	17 (38.6%)	
400-800cm3	1(1.3%)	4 (15.4%)	8 (18.2%)	
>800cm3	0	2 (7.7%)	5 (11.4%)	

[a]pearson chi-squared test, [b]Fisher exact test, [c]kruskal-wallis

Table-4: comparison between adenomyosis group and fibroid group

Variable	p-value	OR(95%CI)
Chronic pelvic pain	0.003	3.1(1.4-7.04)
Normal size uterus	0.04	0.3(0.12-0.9)
Menopause	0.03	3.8(0.8-18.3)
Irregular cycle	0.012	2.6(1.1-6.4)
Tender uterus	0.00002	8.09(2.6-25.1)

Chi square test

OR,odds ratio of adenomyosis group relative to the odds of fibroid alone group: CI, confidence interval

regress after menopause but not adenomyosis.

Our study suggests that women with adenomyosis and fibroid have smaller size of uterus as well as smaller fibroid when compared to women with fibroid alone which suggest that adenomyosis is contributing to symptomatology which leads to hysterectomy. Thus if the women had symptoms that is disproportionate to size of fibroid, gynecologists may think about the presence of adenomyosis as differential diagnosis.

Bergholt T et al showed significant association with adenomyosis and endometrial hyperplasia but we could not find such association rather we found more of proliferative type of endometrium in hysterectomy specimen with adenomyosis alone.[6] However 31.1% of women with fibroid alone had endometrial hyperplasia suggesting that both fibroid and endometrial hyperplasia is estrogen dependent.

Thus from this study we can conclude that adenomyosis is more frequent among women reporting dysmenorrhoea, menometrorrhagia, chronic pelvic pain and along with bulky uterus. Women with fibroid alone has more of menorrhagia than pain and is associated with enlarge uterus. If women have small fibroid uterus but have more symptoms – think about co-existence of "ADENOMYOSIS".

REFERENCES

1. Paula J.Adams Hilllard. Benign diseases of the female reproductive tract: symptoms and signs. In: Jonathan S. Berek,eds, Novak's Gynecology,13th edn. philadelphia :Lippincott Williams & Wilkins 2002: 428, 435.
2. Shaikh H, Khan KS. Adenomyosis in Pakistani women: four year experience at the Aga Khan University Medical Centre, Karachi. *J Clin Pathol* 1990; 43:817–819.
3. Vercellini P, Parazzini F, Oldani S, Panazza S, Bramante T, Crosignani PG.Adenomyosis at hysterectomy: a study on frequency distribution and patient characteristics. *Hum Reprod* 1995; 10:1160–1162.
4. Parazzini F, Panazza S, Chatenoud L, Oldani S, Crosignani PG. Risk factorsfor adenomyosis. *Hum Reprod* 1997; 12: 1275-9.
5. Vavilis D, Agorastos T, Tzafetas J *et al*. Adenomyosis at hysterectomy: prevalence and relationship to operative findings and reproductive and menstrual factors. *Clin Exp Obstet Gynecol* 1997; 24: 36-8.
6. Bergholt T, Eriksen L, Berendt N, Jacobsen M, Hertz JB. Prevalence and risk factors of adenomyosis at hysterectomy. *Hum Reprod* 2001; 16: 2418-21.
7. Weiss G, Maseelall P, Schott LL, Brockwell SE, Schocken M, Johnston JM. Adenomyosis a variant, not a disease? Evidence from hysterectomized menopausal women in the Study of Women's Health Across the Nation (SWAN). *Fertil Steril* 2009; 91: 201-6.
8. Goodwin SC, McLucas B, Lee M *et al*. Uterine artery embolization for the treatment of uterine leiomyomata midterm results. *J Vasc Interv Radiol* 1999; 10: 1159-65.
9. Doyle JO, Betjes H, Missmer SA, Fennessy FM, Tempany CMC, Stewart EA. MRI-guided focused ultrasound ablation (MRgFUS) of uterine fibroids: clinical predictors of successful outcome at three years.. *Fertil Steril* 2007; 88:S82.
10. Pandis N, Karaiskos C, Bardi G *et al*. Chromosome analysis of uterine adenomyosis. Detection of the leiomyoma- associated del (7q) in three cases. *Cancer Genet Cytogenet* 1995; 80: 118-20.
11. Anania CA, Stewart EA, Quade BJ, Hill JA, Nowak RA. Expression of the fibroblast growth factor receptor in women with leiomyomas and abnormaluterine bleeding. *Mol Hum Reprod* 1997; 3: 685-91.
12. Propst AM, Quade BJ, Gargiulo AR, Nowak RA, Stewart EA. Adenomyosis demonstrates increased expression of the basic fibroblast growth factor receptor/ ligand system compared with autologous endometrium. *Menopause* 2001; 8: 368-71.
13. Merrill JA, Creasman WT. Disorders of the uterine corpus. In Scott JR, Di Saia PJ, Hammond CB *et al*. (eds), Danforth's Obstetrics and Gynecology. 6th edn. Philadelphia: J.B. Lippincott, 1990: 1023.
14. Owolabi TO, Strickler RC. Adenomyosis. A neglected diagnosis. *Obstet Gynecol* 1977; 50: 424-7.
15. Vercellini P, Ragni G, Trespidi L *et al*. Adenomyosis: a de´ja` vu? *Obstet. Gynecol Surv* 1993; 48: 789-94.
16. Vercellini P, Vigano P, Somigliana E, Daguati R, Abbiati A, Fedele L. Adenomyosis: epidemiological factors. *Best Pract Res Clin Obstet Gynaecol* 2006; 20:465–77.
17. Pron G, Cohen M, Soucie J, Garvin G, Vanderburgh L, Bell S. The Ontario Uterine Fibroid Embolization Trial. Part 1. Baseline patient characteristics, fibroid burden, and impact on life. *Fertil Steril* 2003; 79: 112-9.
18. Edwards RD, Moss JG, Lumsden MA *et al*. Uterine-artery embolization versus surgery for symptomatic uterine fibroids. *New Engl J Med* 2007; 356: 360-70.
19. Taran FA, Weaver AL, Coddington CC, Stewart EA. Characteristics indicating adenomyosis coexisting with eiomyomas: a case–control study. *Human Reproduction* 2010; 25: 1177-82.
20. Azziz R. Adenomyosis: current perspectives. *Obstet Gynecol Clin North Amer* 1989; 16: 221-35.
21. Fraser IS, McCarron G, Markham R, Resta T, Watts A. Measured menstrual blood loss in women with menorrhagia associated with pelvic disease or coagulation disorder. *Obstet Gynecol* 1986; 68: 630-3.
22. Molitor, J.J. Adenomyosis: a clinical and pathologic appraisal. *Amer J Obstet Gynecol* 1971; 110: 275-84.
23. Marshall LM, Spiegelman D, Goldman MB. A prospective study of reproductive factors and oral contraceptive use in relation to the risk of uterine leiomyomata. *Fertil Steril* 1998; 70: 432-9.
24. Walker CL, Cesen-Cummings K, Houle C, Baird D, Barrett JC, Davis B. Protective effect of pregnancy for development of uterine leiomyoma. *Carcinogenesis* 2001; 22: 2049-52.
25. Parazzini F. Risk factors for clinically diagnosed uterine fibroids in women around menopause. *Maturitas* 2006; 55: 174-9.