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A Challenge in Management of Adenomyosis in Mosul City

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ABSTRACT

Adenomyosis is an important clinical challenge in gynecology and health care economics in it is fully developed form, TAH is often used to treat almost major of cases. Moreover, adenomyosis and leiomyomas may be commonly coexist in the same uterus so differentiating the symptoms for each process can be problematic although update treatment in other countries as MRI guided focused ultrasound may promise in treating such cases. Objective: summarize all the factors that may cause, deal with, and or decline adenomyosis as epidemiological factors, phenotypes, social state, and how we dealt with patient complaint and what available in our country on post war period. Setting: It carry out on our private clinic and Al-Zahrawy private hospital for one year from March 2018 to March 2019. Patient and method: A descriptive study was carried out for about one year follow up starting with a good history, investigation, and conclusion for sixty patients. Results: there are a significant and direct correlation between the occurrence of adenomyosis and age, parity and ethnicity of patients. We faced many challenges when doing this study as a diagnosis and surgical management and for the follow up the patients with limited available facility on post war period. Conclusion: Adenomyosis was found to be most histopathological finding retrospectively.

Keywords: Adenomyosis, leiomyomas, TAH Sample.

INTRODUCTION

Adenomyosis is defined as the benign invasion by the endometrium into the myometrium. Both endometrial glands and endometrial stroma must be present and some pathologists also consider that these should be surrounded by hypertrophic hyperplastic musculature. Such features typically result in significant uterine enlargement. Since the endomyometrial border is irregular, the definition usually includes a depth of penetration between 2.5 and 5 mm. Alternatively, it can be determined in terms of microscope fields, with one low - power field being equivalent to 1 cm [1] . Since the symptoms appear to be related to the depth of penetration, it would seem reasonable to include only those with a greater degree of invasion. The result is an enlarged uterus in which the adenomyosis may be either diffuse or present as focal deposits or adenomyomas [1].

Cystic Adenomyoma:

Rarely, adenomyosis may present as a cystic lesion lined with endometrial tissue and surrounded by myometrial tissue when it is called “cystic adenomyoma.” Juvenile cystic adenomyoma (JCA) is a subgroup of cystic adenomyoma that commonly occurs in adolescents or women <30 years of age and is not associated with diffuse adenomyosis. They found that laparoscopic excision of the lesion demonstrated significant improvement of dysmenorrhea in these cases [4].

Pathology:

The exact pathogenesis of adenomyosis remains debatable. The diagnosis of adenomyosis is made when ectopi endometrial implants are found within the myometrium of the uterus. The most common and widely accepted theory involves the downward invagination of the endometrial basalis layer into the myometrium due to either myometrial weakness or altered immunologic activity leading to disruption of the endometrial myometrial interface, also known as the “junctional zone (JZ)”.

Leyendecker etal. showed that uterine auto-traumatisation and the initiation of the mechanism of tissue injury and repair (TIAR) as the primary cause for adenomyosis development based on their method of “visualization” by transvaginal ultrasound (TVS) and cinematographic magnetic resonance imaging (MRI). Their group showed the archimetral

compression from the neometral contraction at the onset of menstruation causes high intrauterine pressure, leading to rupture of the archi myometrium at cornual angles. thus, fragments of the basal endometrium are then detached and deposited into the myometrial wall where they develop into endometriotic cysts. In addition, as the basal stromal cells at the fundo-cornual raphe are chronically over stretched, it initiates the TIAR mechanism and development of an adenomyomas. Other theories include de novo development from embryonic-misplaced pluripotent Mullerian remnants or invagination along the intramyometrial lymphatic system or displaced bone marrow stem cells [4].

Incidence:

The incidence of adenomyosis reported in the literature varies considerably between 8% and 61%, the preoperative diagnosis usually being less than 10%. It is therefore predominantly a post - hysterectomy (in 15 – 30%) diagnosis and some discrepancy is likely to result from the varying diagnostic methodologies used by different pathologists [1].

Aetiology

The ectopic endometrium is responsive to steroid hormones. In addition, gene polymorphisms have been identified in the oestrogen receptor with mutations of estrogen receptor alpha. This ectopic tissue may respond to the cyclical hormone changes of the menstrual cycle which contributes to the symptoms of heavy menstrual bleeding (HMB) and dysmenorrhoea. Abnormal prostaglandin production also occurs and this could exacerbate both pelvic pain and heavy bleeding. These symptoms are associated with a gradually enlarging uterus, a finding which is unlikely to be picked up clinically unless serial vaginal examinations are performed [1]. Adenomyosis is increasingly being viewed as a separate pathological entity affecting a different population of patients with an as yet unknown and different aetiology [2].

Clinical presentation:

The classic presentation of adenomyosis is heavy, painful menstrual bleeding, typically occurring in multiparous women between 40 and 50 years of age [6]. Heavy menstrual bleeding is present in up to 40–60% of patients, which may be due to the enlarged endometrial surface area or the increased vascularity of the endometrium [7]. Dysmenorrhea occurs in 15–30% of patients, which may be related to the swelling of endometrial tissue within the myometrium or increased production of prostaglandin within the myometrium [8].

Both the amount of bleeding and degree of pain were shown to be significantly correlated with the degree of myometrial invasion [7]. Other presenting features include chronic pelvic pain, dyspareunia, and the finding of an enlarged uterus in an asymptomatic subject. Women with adenomyosis had been shown to have a decreased quality of life [9]. up to 33% of patients may be asymptomatic, and the diagnosis of up to 30% of patients was only made by histology following a hysterectomy [10].

There is also increasing evidence to show an association between infertility and adenomyosis [11]. Several mechanisms may be involved, including impairment of sperm transport [8], aberrant uterine contractility [11], alterations of adhesion molecules, cell proliferation, apoptosis, and free radical metabolism [12].Adenomyosis is also speculated to be a cause of recurrent implantation failure during IVF treatment [9]. The commonest presentation is that of HMB associated with significant dysmenorrhoea, the latter being worse in deep infiltrating disease [13].The condition is characteristic of the fifth decade of life, with 45 years being the commonest age of presentation. It is very rare in nulliparous women and occurs less frequently in smokers [14].

Diagnosis

The diagnosis is normally made on histological examination of the uterus after hysterectomy [1]. Examination of patients may be useful with the findings most often of a bulky and sometimes tender uterus, particularly if examined perimenopausally. Ultrasound examination of the uterus may be helpful on occasions when adenomyosis is particularly marked or localized, haemorrhage filled, distended endometrial glands. In some instances where there is a very localized area of adenomyosis, this may give an irregular nodular development within the uterus, very similar to that of uterine fibroids[1].

However, magnetic resonance imaging (MRI) has been shown to be more accurate than ultrasound in diagnosing adenomyosis as shown in "Fig.1". This modality enables the clinician to distinguish adenomyosis from other pathologies such as uterine fibroids, which may also present with an enlarged uterus [1]. MRI provides excellent images of myometrium, endometrium and areas of adenomyosis and is now the investigation of choice [2]. More often, however, transvaginal ultrasound (TVS) is used as the primary and only investigative tool for women with suspected adenomyosis. Early diagnosis can impact significantly on the choice of treatment offered to an individual patient [1].

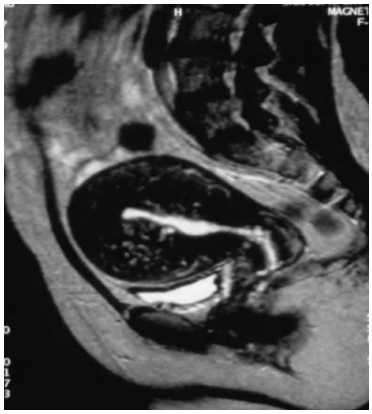

Figure. 1: Diffuse adenomyosis of the uterus. By kind permission of Dr. Nigel McMillan, Consultant Radiologist, The Western Infirmary, Glasgow, UK.

Histological examination is the gold standard in the diagnosis of adenomyosis, even though the exact histological criteria have not been universally agreed. One accepted criterion is the presence of endometrial tissue more than 2.5 mm below the endomyometrial junction or a JZ thickness of more than 12 mm [15]. The modification of the uterine structure may range from thickening of the JZ of >12 mm to nodular or diffuse lesions involving the entire uterus. Thus, adenomyosis is classified to "diffuse adenomyosis" where endometrial deposits are found dispersed within the myometrium or "focal adenomyoma" where the endometrial deposits are more localized at one site within the uterine wall as a confined lesion. Apart from the findings of these ectopic endometrial tissues within the myometrium, smooth muscle changes like hyperplasia are often found. Ultrastructural difference between smooth muscle cells from adenomyosis and normal uterus were found with myocytes showing cellular hypertrophy, differences in cytoplasmic organelles, nuclear structures, and intercellular junctions [13]. The myocytes in adenomyosis also lack the cyclical changes present in myocytes of the normal uterus.

Two-dimensional (2D) Transabdominal USG may reveal uterine enlargement or asymmetric thickening of the anterior and posterior myometrial walls. However, transabdominal USG is often not accurate enough in diagnosing adenomyosis as it fails to provide sufficient image resolution for visualization of the myometrium. Therefore, 2D transvaginal USG is often the first-line investigation. In a review performed by Reinhold et al., it was shown that transvaginal USG had a sensitivity of 80–86%, specificity of 50–96%, and an overall accuracy of 68–86% in diagnosing diffuse adenomyosis [15].USG features of adenomyosis include the presence of three or more sonographic criteria: heterogeneity, increased echogenicity, decreased echogenicity, and anechoic lacunae or myometrial cysts [17]. In contrast to uterine fibroids, adenomyomas has a more elliptical shaped lesion with poorly defined borders, no calcifications, or edge shadowing. In doubtful cases, Doppler sonography may be helpful in that blood vessels in the case of adenomyomas usually follow their normal vertical course in the myometrial areas while in the case of uterine fibroid, blood vessels are usually located in the periphery[15]. Sonographic diagnosis of adenomyosis is not always easy but the consensus statement and recommendation published by the MUSA (Morphological Uterus Sonographic Assessment) group on how sonographic features of adenomyosis should be described and measured should help to improve the diagnostic accuracy[15].

Three-dimensional (3D) USG improves diagnostic accuracy of adenomyosis as it allows better imaging of the JZ [19]. The JZ is often visible as a hypoechogenic sub endometrial halo which is composed of longitudinal and circular closely packed smooth muscle fibers. Upon 3D USG, adenomyosis is characterized by a thickened or irregular JZ [20]. Ahmadi and Haghighi showed the accuracy of 3D transvaginal USG in the diagnosis of adenomyosis to be 80% and a positive predictive value of 95% based on the detection of an irregular JZ on coronal plane. Exacoustos et al. (21) analyzed a total of 72 premenopausal patients with 2D and 3D transvaginal USG before hysterectomy. In the study, the histological prevalence of adenomyosis was 44.4%. Their group agrees that the coronal section of the uterus obtained by 3D transvaginal USG allows accurate evaluation and measurement of the JZ and its alteration shows good diagnostic accuracy for adenomyosis. T

hey showed that the presence of myometrial cysts was the most specific 2D transvaginal USG feature with specificity of 98% and accuracy of 78% while heterogeneous myometrium was the most sensitive feature with a sensitivity of 88% and accuracy of 75%. As for 3D transvaginal USG, with a JZ difference of more than or equal to 4 mm, JZ infiltration and distortion had a high sensitivity of 88% and the best accuracy of 85% and 82%, respectively. The overall accuracy of diagnosing adenomyosis for 2D and 3D transvaginal USG was 83% and 89%, sensitivity was 75% and 91%, specificity was 90% and 88%, positive predictive value was 86% and 85%, and negative predictive value was 82% and 92%, respectively. 3D USG also has the advantage of allowing storage of the images with subsequent offline manipulation and interpretation.

Magnetic resonance imaging (MRI) is the gold standard imaging modality for assessing the JZ in the evaluation of adenomyosis[22] The common features of adenomyosis on MRI include [1] thickening of the JZ, JZ thickness ≥12 mm, or irregular Junctional thickness with a difference of >5 mm between the maximum thickness and the minimum thickness, (2) an ill-defined area of low signal intensity in the myometrium on T2-weighted MR images, and (3) islands of ectopic endometrial tissue identified as punctate foci of high signal intensity on T1-weighted image [23]. However, MRI is expensive and may not be readily available in every unit. Moreover, Reinhold et al. [24]. prospectively studied 119 patients undergoing hysterectomy and compared findings between TVS and MRI.

Table 1: Accuracy of TVS and MRI for the noninvasive diagnosis of adenomyosis.

	TVS	MRI
Sensitivity	72	77
Specificity	81	89
Positive likelihood ratio	3.7	6.5
Negative likelihood ratio	0.3	0.2

The study showed that there was no significant difference in sensitivity and specificity between the two groups. Champaneria et al. [23]. Also performed a systematic review comparing test accuracy between USG and MRI for the diagnosis of adenomyosis. Their study findings are summarized in (Table 1). They agreed that both TVs and MRI show high levels of accuracy for the noninvasive diagnosis of adenomyosis. However, we believe MRI may be particularly useful in the assessment of focal adenomyoma and provides important information on whether surgery should proceed.

Shear Wave Elastography a recent study also showed that using Explorer (Supersonic Imagine, France) scanner with application of shear wave elastography during transvaginal scanning may improve diagnostic accuracy of adenomyosis. This study found that adenomyosis was associated with a significant increase of the myometrial stiffness estimated with shear wave elastography. Further studies are required to verify the clinical usefulness of such an approach [25].

Hysterosalpingography is seldom used to diagnose adenomyosis. However, in patients undergoing infertility assessment, the occasional Finding of speculations measuring 1- 4 mm in length, arising from the endometrium towards the myometrium, or a uterus with the "tuba erecta" finding may be suggestive of adenomyosis [26].
Hysteroscopy several hysteroscopic appearances have been found to be associated with adenomyosis, including irregular endometrium with endometrial defects or superficial openings, hypervascularization, strawberry pattern, or cystic hemorrhagic lesions [27]. Nevertheless, there is limited data available on the diagnostic accuracy of these various features.

Hysteroscopic and Laparoscopic Myometrial Biopsy in 1992, McCausland [28] showed that myometrial biopsies helpful to diagnose adenomyosis. The study found that the depth of adenomyosis was correlated with the severity of menorrhagia. Of the 90 patients studied, 50 patients had normal hysteroscopy in which 55% of them had significant adenomyosis (greater than 1 mm) when compared to controls (0.8mm). In that study, it was suggested that minimal adenomyosis may be treated definitively by endometrial ablation while deep adenomyosis should be treated by hysterectomy. They also showed that endometrial glands under a scar Could not only bleed and cause pain but also have malignant potential.

The authors suggested routine myometrial biopsy at the time of operative hysterectomy should be considered. However, Darwish et al. [29] showed hysteroscopic myometrial biopsies using rigid biopsy forceps to be inadequate and did not recommend its use. Popp et al. (30) showed that the sensitivity of a single myometrial biopsy in diagnosing adenomyosis ranged from 8 to 18.7%, while the specificity was 100 % among 680 biopsy specimens in 68 surgically removed uterus using automatic cutting needle sampling. Gordts et al. [31] recommended the use of hysteroscopic guided biopsy for the diagnosis of adenomyosis using a new device, the UteroSpirotome. It can also be used under ultrasound guidance to get access to small cystic adenomyoma lesions.

Laparoscopic Myometrial Biopsy in a prospective, non-randomized study conducted by Jeng et al. [32] evaluating 100 patients with clinical signs and symptoms strongly suggestive of adenomyosis, the sensitivity of myometrial biopsy was 98% and the specificity 100%; the positive predictive value was 100% and the negative predictive value 80%, which were superior to those of transvaginal sonography, serum CA-125 determination, or the combination of both. The group suggested that laparoscopy-guided myometrial biopsy is a valuable tool in the diagnosis of diffuse adenomyosis in women presenting with infertility, dysmenorrhea, or chronic pelvic pain.

Treatment

As in the case of endometriosis, the management strategy of adenomyosis depends primarily on the presenting symptom and whether it is associated with reproductive failure. Management of Menstrual Symptoms.

***Medical Treatment*:** Medical treatment for adenomyosis is similar to those given for endometriosis. Apart from symptomatic relief, hormonal treatment mainly works by inhibition of ovulation, cessation of menses, improving the hormonal milieu, and causing decidualization of the endometrial deposits.

Analgesic (*Nonsteroidal anti-inflammatory drugs (NSAIDs)*) work by inhibiting the cyclooxygenase (COX-1 and COX-2) and decreasing the production of prostaglandins. NSAIDs have been proved to be effective in treatment of primary dysmenorrhea by Gambone et al. [33]. It is usually the first-line treatment for symptomatic pain relief for adenomyosis.

Oral Contraceptive Pills (OCPs): work by inhibiting ovulation by suppressing the release of gonadotrophins. Many studies have shown that they are effective in the treatment of dysmenorrhea. A prospective observational trial showed that continuous low-dose OCP were more effective than cyclical low-dose OCP in controlling symptoms in patients after surgical treatment for Endometriosis [34]. Mansouri et al. [35]. have shown regression of adenomyosis on MRI after using oral contraceptive pills for 3 years in adolescents with adenomyosis presenting with chronic pelvic pain.

***Danazol*:** is an isoxazole derivative of 12 alpha-ethinyl testosterone. It causes a hypogonadic state and thus is widely used for treatment of endometriosis and abnormal uterine bleeding [36]. However, data on its use in adenomyosis remains limited. This may be due to its unwanted adverse effects after systemic treatment. In 2000, Igarashi et al. [37] reported a novel conservative medical therapy for uterine adenomyosis with a danazol-loaded intrauterine device in 14 women. During insertion of the danazol-loaded IUD, there was complete remission of dysmenorrhea in 9 patients, reduction in 4, and no change in 1 patient. There was complete remission of hypermenorrhea in 12 patients and no change in 2. Nine out of 14 patients also showed reduction in the maximum thickness of the myometrium as measured by MRI. However, further studies are required to confirm the clinical usefulness of the treatment.

***Dienogest*:** is a selective synthetic oral progestin that combines the pharmacological properties of 17-alpha-progesterone and 19 nor progesterone with pronounced local effect on endometrial tissue. Dienogest has been shown to be effective in the treatment of endometriosis-associated pelvic pain. A prospective clinical trial has shown dienogest to be a valuable alternative to depot triptorelin acetate for treatment of premenopausal pelvic pains in women with uterine adenomyosis. The study included a total of 41 patients with adenomyosis with pelvic pain and menorrhagia. The patients were allocated to receive oral dienogest (2 mg/day) or triptorelin acetate (3.75 mg/4 weeks) for 16 weeks. Both treatments were highly effective in treatment of dysmenorrhea, dyspareunia, and chronic pelvic pain associated with adenomyosis, although triptorelin acetate appeared superior to dienogest in controlling menorrhagia [38].

Levonorgestrel-Releasing Intrauterine Device (LNG-IUD): is an intrauterine device, which release 20 micrograms of levonorgestrel per day. It has been shown to be an effective treatment for abnormal uterine bleeding. LNG-IUD acts locally and causes decidualization of the endometrium and adenomyotic deposits. LNG-IUD alleviates dysmenorrhea by improving uterine contractility and reducing local prostaglandin production within the endometrium. LNG-IUD appears to be an effective method in relieving dysmenorrhea associated with adenomyosis [39] and more effective than the combined OC pill [40], improved the quality of life [42], and appears to be a promising alternative treatment to hysterectomy. LNG-IUD may be used in conjunction with other treatment modalities such as GnRH analogue [42] or transcervical resection of the endometrium (TCRE) [43]. In the latter study, it was found that TCRE combined with LNG-IUD was more effective in reducing menstrual flow compared with the LNG- IUD alone although there was no significant difference in the amount of pain reduction between the two treatment strategies.

***GnRH Agonists*:** are effective in alleviating dysmenorrhea and relieving menorrhagia associated with adenomyosis [44]. However, due to the undesirable climacteric side effects and risk of osteoporosis, treatment with GnRH agonists is usually restricted to a short duration of 3–6 months although the duration of use may be extended if add-back estrogen therapy is employed [45]. Discontinuation of treatment usually leads to regrowth of The lesions and recurrence of symptoms.

Selective Estrogen Receptor Modulator (SERM): like tamoxifen or raloxifene have been tried in the treatment of endometriosis [46]. based on observations that SERMs may reduce endometriosis lesion in mouse [46]; however, their value in the treatment of adenomyoma has not been formally explored.

***Aromatase Inhibitors*:** Like endometriosis, adenomyotic deposits are estrogen-dependent. Aromatase inhibitors inhibit the conversion of estrogen from androgens, thereby lowering the synthesis of estrogen. A prospective randomized controlled study found that the efficacy of aromatase inhibitors (letrozole 2.5 mg/day) in reducing the volume of adenomyoma as well as improving adenomyosis symptoms was similar to that of GnRH agonists (goserelin 3.6 mg/month) [48]. Kimura et al. also reported on the combined use of aromatase inhibitors with GnRH agonist with good results in a 34-year-old woman with severe uterine adenomyosis who wished to preserve fertility [49]. They found a reduction in uterine volume of 60% after 8 weeks of treatment as determined by magnetic resonance imaging and ultrasound.

Ulipristal Acetate (UPA): is a potent selective progesterone receptor modulator. There is good evidence to suggest that it can be used to shrink fibroid and control menorrhagia [49]. It is possible that it may be similarly effective in the treatment of adenomyoma but literature data is lacking.

***Antiplatelet therapy*:** there is new evidence to suggest a role of antiplatelet therapy in treating adenomyosis. Emerging evidence suggests that endometriotic lesions are wounds undergoing repeated tissue injury and repair (ReTIAR), and platelets induce epithelial-mesenchymal transition (EMT) and fibroblast-to-myofibroblast transdifferentiation (FMT), leading ultimately to fibrosis. Adenomyotic lesions are thought to have similar pathogenesis to that of endometriosis. A recent study in mice suggests that antiplatelet treatment may suppress myometrial infiltration, improve generalized hyperalgesia, and reduce uterine hyperactivity [50].

Uterine Artery Embolization (UAE): has been used to treat symptomatic fibroids since the 1990s. There is increasing evidence to suggest that it is also effective in the treatment of management of adenomyosis. In a review of 15 studies including 511 women with adenomyosis, Popovic et al. found (51) significant clinical and symptomatic improvement in 75% of subjects at short- and long-term follow-up. A recent retrospective observational study of 252 patients who underwent UAE with up to 5 years of follow-up showed that improvement in dysmenorrhea and menorrhagia are more likely to occur in vascular lesions.

High Intensity Focused Ultrasound (HIFU): is another nonsurgical treatment for uterine fibroids that focuses high-intensity ultrasound in the target lesion causing coagulative necrosis and shrinkage of the lesion. Both MRI and USG can be used for guidance for the procedure. MRI has better real-time thermal mapping during the HIFU treatment. Yet, ultrasound-guided HIFU is less costly and other real-time anatomic monitoring imaging and a grey scale change during treatment represents a reliable indicator in treatment response. It is effective in both focal and diffuse lesions. Ultrasound-guided HIFU was n shown to be technically successful in up to94.6%of patients in a review of 2549 patients among 10 different centers with symptomatic adenomyosis [52].

Endomyometrial Ablation or Resection: there is limited report on the use of laparoscopic or hysteroscopic endometrial in treating adenomyosis in the literature. The success rate of myometrial electrocoagulation ranges from 55 to 70% as reported [53].Wood [54] reported success in 4 out of 7 patients who underwent myometrial electrocoagulation,

While Phillips et al. [55] had 7out of 10 patients with symptomatic adenomyosis diagnosed by MRI treated with laparoscopic bipolar coagulation, having significant reduction or resolution of dysmenorrhea or heavy menstrual bleeding.

***Hysterectomy*:** is the definitive treatment option for intractable symptomatic adenomyosis when medical or other conservative treatments have failed to control the symptoms. Patients undergoing hysterectomy for adenomyosis should be advised of an increased risk of bladder injury and persistent pelvic pain. Furuhashi et al. [56] reviewed 1246 vaginal hysterectomies and found that patients undergoing vaginal hysterectomy for adenomyosis have increased risk of bladder injury compared with those performed for leiomyoma (2.3% versus 0.7%). It may be a result of difficulty in identifying the supravaginal septum and the vesicovaginal or vesicocervical planes. Several studies have reported on persistent pelvic pain after hysterectomy for adenomyosis.

Once a decision to proceed with hysterectomy has been made, the possibility of oophorectomy should be discussed. In general, it is not considered necessary to routinely remove the ovaries in premenopausal women, but it may be indicated in women who suffer from cyclical symptoms, with concomitant ovarian endometriosis, or who are considered to have an increased risk of developing ovarian cancer, including those with a family history of the condition. Interestingly, a recent population-based study by Kok et al. [57] suggested that the risk of developing ovarian cancer in women with newly diagnosed adenomyosis is increased by 4-5 fold. If the finding is confirmed, there is a strong case to consider prophylactic oophorectomy at the time of hysterectomy for adenomyosis in premenopausal women.

Aims of the study

- To assess the challenge that doctors faced when dealing with patients with adenomyosis, our statistics involved a good survey for the disease, minimal access surgical methods should be as much as possible and advanced technique in radiological equipment should use.

MATERIAL AND METHODS

- This was a quantitative prospective design involving 60 women. The methodology applied in this study involves direct questioning using questionnaires, and in addition to clinical assessment of the patients. A study was done at private clinic and hospital from the beginning of March 2018 to the end of March 2019.
- Information on age, education, parity, occupation, obstetrics, medical and surgical history was obtained from the women using a close-ended questionnaire.

Patients selection:

The women were selected while attending our private clinic for assessment and management.

Inclusion criteria:

Any women with diagnosed case or suspected case of adenomyosis from 30 to more than 60 years old which are that most of cases founded in this age groups.

Exclusion criteria:

Women who refuse to participate in the study , severity ill patient and patient with severe liver or renal diseases

All the participants were subjected to:

They were told about the nature of the study and only those who agreed to participate in the study were included. Verbal consent was obtained from all women in the study. Information's about the age of the patient, parity, medical, surgical and past obstetric history were taken from all participants. Physical and pelvic examination was performed to all participants include: review of vital signs, abdominal examination and pelvic examination.

Body mass index was calculated to all patients by dividing the weight of participant in kilograms over the square of the height in meters. Every patient had undergone the following investigations in the form of : sugar profile, hemoglobin level, general urine examination, lab. Test: for tumor history patient or for other medical illnesses, radiological: ultrasound, Doppler and MRI and histopathology: for dilatation and curettage and TAH samples.

Study method:

A descriptive study was carried out to 60 patients on private clinic, for about 1 year.

Statistical analysis:

Data were analyzed using the computer facility with use of SPSS – 18 (statistical package for social sciences version 18 "PASW") software package. Data were presented in simple measures of number, frequency, percentage, mean, range and standard deviation.

Significance of difference between percentages (for qualitative data) was measured using chi-squared test. P value less than 0.05 was considered as the level of significance.

RESULTS

This was a quantitative prospective design involving 60 women. The methodology applied in this study involves direct questioning using questionnaires, and in addition to clinical assessment of the patients. A study was done at private clinic and hospital from the beginning of March 2018 to the end of March 2019. Information on age, education, parity, occupation, obstetric, medical and surgical history was obtained from the women using a close-ended questionnaire.

Table 2 showed the following:

The mean age of patients with adenomyosis was (43.33) years and the range were (3). There was significant correlation between patient age and the occurrence of adenomyosis as the p-value < 0.0001. The mean parity of patients with adenomyosis was (13.067) babies and the range were (1). There was significant correlation between increase parity and occurrence of adenomyosis as the p-value <0.0001.

There was increased incidence of adenomyosis in Muslim ladies in compares with other ethnicity and there was significant correlation between them as the p-value < 0.0001.

There was increased incidence of adenomyosis in obese patient (as their BMI >30kg/m^2) and the correlation was significant as the p-value < 0.02.

There was decreased incidence of adenomyosis with cigarette smoking and the correlation was found significant between nonsmoking and occurrence of adenomyosis as the p-value < 0.0001.

There was strong and direct correlation between the hypertension and occurrence of adenomyosis in same patient in compares with non-medical or other medical illness and the correlation was found significant between the hypertension and occurrence of adenomyosis as the p-value < 0.0001.

There was strong correlation between normal vaginal delivery and occurrence of adenomyosis with mean incidence of about (29.70%) and the correlation was significant between the normal vaginal delivery and adenomyosis as the p-value <0.0001.

There was strong correlation between the dilatation and curettage and the occurrence of adenomyosis with the incidence (27.3%) and the correlation was significant was found as the p-value < 0.0001.

There was correlation between mean age of menarche (10-15 years) and the occurrence of adenomyosis with incidence (91.90%) and the correlation was found significant as the p-value < 0.0001.

There was no correlation between the use of contraceptive and the occurrence of the adenomyosis as the correlation was not significant as the p-value < 0.07.
There was no significant correlation between immigration and the occurrence of adenomyosis as it was found the correlation between the two was not significant as the p-value <0.07.

There strong correlation between the previous occurrence of gynecological illness and the occurrence of adenomyosis especially fibroid with incidence (43.3) and the correlation was significant as the p-value < 0.0001.

Table 2: the correlation between the adenomyosis and different patients parameters.

Characteristics	No. (%)	Chi-square P-value
Age group		43.33 , DF=3 <0.0001
30 – 39 years	2 (3.3%)	
40 – 49 years	21 (35.0%)	
50 – 59 years	33 (55.0%)	
60 + years	4 (6.7%)	
parity		13.067 ,DF=1 <0.0001
>5 babies	44 (73.3%)	
< 5 babies	16 (26.7%)	
Ethnicity		7 , DF=1 <0.0001
Muslim	56 (93.3%)	
Other	4 (6.7%)	
BMI		5.40 , DF=1 <0.02
<28 kg/m²	21 (35.0%)	
>30 kg/m²	39 (65.0%)	
smoking		44.10 , DF=2 <0.0001
<10 cigarette /day	11(18.3%)	
>20 cigarette/day	5 (8.3%)	
Non- smoker	44 (73.3%)	
Medical illness		24.7 , DF=3 <0.0001
Hypertensive	33 (56.7%)	
Diabetes	3 (5.0%)	
Other	1	
Null	23 (38.7%)	
Type of delivery		29.70 , DF=1 <0.0001
NVD	47 (78.3%)	
C- section	13 (21.7%)	
Abortion		27.3 , DF=2 <0.0001
Spontaneous	21 (35.0%)	
Ectopic	3 (5.0%)	
D&C	36 (60.0%)	
Age of MC		91.90 , DF=2 <0.0001

<10 years	3 (5.0%)	
10 – 15 years	55 (91.7%)	
>15 years	2 (3.3%)	
contraceptive		3.26 , DF=1 0.07
IUCD	23 (38.3%)	
Other	37 (61.7%)	
Immigration state		3.26 , DF=1 0.07
Immigrant	37 (61.7%)	
Not	23 (38.3%)	
Previous diseases		43.3 , DF=2 <0.0001
Endometriosis	9 (15.0%)	
Fibrosis	44 (73.3%)	
Null	7 (11.7%)	

DISCUSSION

Adenomyosis was historically believed to be a disease of multiparous women. However, with advances in diagnostic technology and the rising age at which women approach motherhood, it is being increasingly seen in women attending fertility clinics (58). Histologically, it is identified as the presence of heterotopic endometrial glands and stroma within the myometrium with adjacent hyperplasia of the myometrium [59]. Adenomyosis can be diffuse or focal. Diffuse disease is most commonly located in the posterior uterine wall, where it can be subdivided into superficial and deep (extending more than one-third of the way into the myometrium) disease. Adenomyosis can also be focal, characterized by nodules in the Junctional zone (JZ—junction between endometrium and inner myometrium) or myometrium (adenomyomas). It is usually diagnosed between 40 and 50 years, with the most common presenting symptoms being dysmenorrhoea, menorrhagia, and subfertility. Adenomyosis is notoriously difficult to diagnose clinically and in the past has been diagnosed on histology after hysterectomy [60] Adenomyosis is often misdiagnosed as multiple uterine leiomyoma, which have different prognosis and management options. With greater awareness of the condition and more expert use of technology, such as MRI, the disease is now more commonly diagnosed prior to invasive surgery.

In retrospect, one could note that leiomyoma is more likely to be associated with menorrhagia rather than dysmenorrhoea alone. Additionally, on examination, a bulky uterus was noted rather than a nodular uterus, which is more frequently the case with leiomyoma [61]

Moreover, distinguishing superficial from deep adenomyosis remains a challenge, but one that is the key to appropriate management of the condition. Clinically, distinguishing the two remains difficult due to the absence or non-specific nature of symptoms. It is hypothesized that superficial adenomyosis is more commonly associated with abnormal uterine bleeding, whereas the deeper disease is thought to cause more pain, heavier bleeding, and dyspareunia. On examination, the uterus is globular and painful on mobilizing.

Table 3: the prevalence of adenomyosis after hysterectomy specimens for various gynecological condition

study	Vercellini et al. 1995	Vavilis et al. 1997	Sideman and Kjerurlff 1996	Parazzini et al. 1997	Bergholt et al. 2001
No. of cases	**1334**	**594**	**1252**	**707**	**549**
adenomyosis	**25**	**20**	**12- 58**	**21**	**10- 18**
Uterine fibroid	**23**	**21**		**15**	
Genital prolapse	**26**	**26**		**30**	
Ovarian cyst	**21**	**18**		**30**	
Cervical cancer	**19**	**18**		**25**	
Endometrial cancer	**28**	**16**			
Ovarian cancer	**28**	**21**			

Challenge in management of adenomyosis:

The management of adenomyosis remains a great challenge to practicing gynecologists. Until recently, hysterectomy has been the only definitive treatment in women who have completed childbearing. A number of nonsurgical and minimally invasive, fertility-sparing surgical treatment options have recently been developed. Adenomyosis is a common benign gynecological condition but its diagnosis and treatment remain a clinical challenge to physicians. The true incidence of adenomyosis is unknown and the prevalence varies widely due to the lack of a standardized definition

and diagnostic criteria. The prevalence from previous retrospective cohort and prospective cohort observational studies is summarized in Table 3. Adenomyosis also commonly occurs together with endometriosis. Di Donato et al.[61] showed a prevalence of 21.8 % in women undergoing surgery for endometriosis. They also showed an association with parous women, increasing age, dysmenorrhea intensity, and presence of deep infiltrating endometriosis. Adenomyosis is best defined as "the benign invasion of endometrium into the myometrium, producing a diffusely enlarged uterus which microscopically exhibits ectopic non-neoplastic, endometrial glands and stroma surrounded by the hypertrophic and hyperplastic myometrium"

Adenomyosis and infertility

Although no direct epidemiological studies exist linking adenomyosis to infertility, a strong argument can be made linking the two from indirect studies. Early data from de Souza *et al* [62] demonstrated a 54% incidence of JZ thickening (strong evidence for adenomyosis) in subfertile patients with symptoms of menorrhagia and dysmenorrhoea. In 2013, Tomasetti and colleagues [63] concluded that adenomyosis confers lifelong infertility in baboons and a poorer outcome after assisted reproduction techniques. They also reported a dose-effect relationship between the extent of adenomyosis and abnormal contractility of the uterus and fallopian tubes. However, the group highlighted the difficulty in assessing the relationship between adenomyosis and subfertility due to the confounding effect of endometriosis that often coexists [63].

CONCLUSION

There was significant and direct correlation between the occurrence of adenomyosis and the age, parity, Muslim ethnicity, BMI, nonsmoking, hypertensive, D and C, and previous fibroid conditions. There was no significant correlation between the occurrence of adenomyosis and contraceptive use and immigration.

Recommendations:

Further research is required to explain the perfect and less invasive and the cheapest way to diagnosis and management of adenomyosis. Further detailed studies are needed to study this subject in larger population.

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