

# Endometriosis of the Kidney and the Urinary Tract Organs an Update

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## Abstract

Endometriosis of urogenital tract organs includes the presence of endometrial glands and stroma within or encompassing the urethra, the urinary bladder, the ureters, the renal pelvis or the kidney. Traditionally, endometriosis of the urinary tract had been iterated to be a rare clinical entity with an incidence of 1% to 5.5% in patients with endometriosis. Nevertheless, some authors had indicated that endometriosis of the urinary tract afflicts the kidney and urinary tract organs more frequently than had been previously presumed, particularly in the scenario of patients who have been afflicted by deep infiltrating endometriosis. It had been iterated in a publication previously that ureteric involvement in of endometriosis had been observed in 14.2% of 315 patients with endometriosis. Other authors in the past had documented a prevalence of urinary tract endometriosis of 19.5% in 221 patients with deep infiltrating endometriosis. These previous documentations may indicate that that the prevalence of urinary tract endometriosis had often been underestimated. In view of the fact that endometriosis of the urethra, urinary bladder, ureter, and the kidney manifests with non-specific symptoms and signs, the diagnosis and management of urinary tract endometriosis had remained a challenge. Early diagnosis of endometriosis afflicting the kidney and urinary tract organs is crucial for the prognosis. When the diagnosis is delayed, endometriosis of the ureter could emanate in the development of serious complications such as stenosis of the ureter, with hydroureter and hydronephrosis and finally loss of kidney function. Some cases of endometriosis had tended to be treated with medicaments; nevertheless, surgery has been regarded as the gold standard in the treatment of patients who had been afflicted by deep infiltrating endometriosis. Many publications had demonstrated the feasibility, effectiveness, as well as safety of the laparoscopic approach. In the case of endometriosis of the ureter, the objective of the treatment has tended to be the release of the ureter from all endometriotic tissue to enable normal function and to avoid morbidity. In the scenario of ureteric obstruction by endometriosis, some of the initial management options do include insertion of percutaneous nephrostomy or insertion of retrograde ureteric stent to maintain renal function preceding the undertaking of definite treatment procedures. Some cases of endometriosis of the ureter had been managed by ureterolysis; nevertheless, it has remained controversial whether ureterolysis is sufficient or whether more invasive methods such as ureterectomy are necessary to prevent recurrence. Treatment of endometriosis of the urinary has tended to consist of complete surgical excision of the urinary bladder lesion. Some authors had pointed out that partial cystectomy does appear to be superior to the undertaking of trans-urethral resection of the urinary bladder lesion demonstrating lower recurrence rates. With the development of minimal invasive surgical procedures, other options that had recently been undertaken by some authors and could be undertaken in the future by other clinicians to attain effective initial results include: cryotherapy, radiofrequency ablation, irreversible electroporation, thermotherapy, and selective angiography and super-selective embolization of the arterial branch supplying the endometriosis lesion if a pathology examination is obtained from biopsy of the specimen preceding the definitive procedure. The manifesting symptoms of urogenital endometriosis are often non-specific. In view of the possibility of serious complications, clinicians including urologists need to be aware of endometriosis of the kidney and urinary tract organs and its management options. Establishment of pre-operative diagnosis of endometriosis of the kidney and urinary tract organs might help in the planning of intra-operative management of the lesion.

**Keywords:** endometriosis; kidney; renal pelvis; ureter; urinary bladder; urethra; biopsy; histopathology; radiology image; ultrasound scan; nephrostomy; excision; minimal invasive procedure; laparoscopy

## Introduction

Endometriosis is a terminology that is used for the presence of ectopic endometrial tissue outside the myometrium. [1] Endometriosis is iterated to afflict 10% to 15% of premenopausal women, who are aged usually between 30 years and 35-years. [1] [2] It has been stated that the median age for diagnosis of extragenital lesions is between 35 years and 40 years, which is about 5 years older than that of genital tract lesions. [1] [3] [4] It has been pointed out that extra genital endometriosis may afflict any tissue. [1] It has also been stated that endometriosis afflicting the renal tract is rare and is usually associated with evidence of previous pelvic endometriosis. Endometriosis of the kidney and upper urinary tract is very rare. It had been pointed out that Marshall [5] had described the first case of renal endometriosis. [1] It has furthermore, been iterated that less than 25 cases of renal endometriosis of the kidney had been reported previously in the literature. [1] Endometriosis of the kidney, and upper urinary tract manifests with non-specific symptoms and signs and without a high-index of suspicion, there is a possibility that the diagnosis could be either delayed or the lesion could be misdiagnosed.

## Aim

To update the literature of endometriosis of the kidney and upper urinary tract organs.

## Methods

Internet databases were searched including: Google; google scholar; yahoo; and PUBMED. The search words that were used included: Endometriosis; Endometriosis of kidney; Renal endometriosis; endometriosis of renal pelvis; endometriosis of ureter; and ureteric endometriosis; endometriosis of bladder; endometriosis of urethra. Seventy-six (76) references were identified which were used to write the article in two parts: (A) Overview, and (B) Miscellaneous narrations and discussions from some case reports, case series, and studies related to endometriosis of the kidney and upper urinary tract organs.

## Results

### [1] OVERVIEW

#### Definition / general statement

- Endometriosis is a terminology that is used for presence of endometrial tissue outside of the endometrium and myometrium, consisting of both endometrial glands and stroma. [6]

#### Essential features

- It has been stated that the essential features of endometriosis include: ectopically located endometrial tissue consisting of at least 2 of the following: endometrial type glands, endometrial type stroma or evidence of chronic haemorrhage. [6]
- Endometriosis is associated with ovarian clear cell carcinoma and endometrioid carcinoma and shares similar molecular alterations. [6]
- It had been iterated that endometriosis in patients without cancer harbours oncogenic mutations in *ARID1A*, *PIK3CA*, *KRAS* and *PPP2R1A*, suggesting a neoplastic nature in some cases [6] [7]
- It has been documented that CD10 immunohistochemistry can be used to confirm the presence of endometrial stroma. [6]

#### Terminology

It has been iterated that the ensuing terminologies had been used for endometriosis: [6]

- Endometriotic cyst / endometrioma: cystic form of endometriosis
- Atypical endometriosis: endometriosis with cytologic atypia or crowded glands lined by atypical epithelium resembling endometrial atypical hyperplasia. [8]

#### Epidemiology

The epidemiology of endometriosis had been summated as follows: [6]

- Endometriosis afflicts 5% to 15% women of reproductive age.
- The peak incidence of endometriosis is between: 30 years and 45 years of age.
- Oestrogen dependent endometriosis; can rarely affect individuals who are assigned male at birth taking large doses of oestrogen. [9]

#### Sites

The sites of the human body that tend to be affected by endometriosis had been summated as follows: [6]

- The Ovary (67%) tends to be affected by endometriosis which tends to be more common or > within the anterior and posterior cul de sac and which is higher or more common (>) in the posterior broad ligaments, uterosacral ligaments and more common of higher than (>) the uterus > fallopian tubes > sigmoid colon and appendix > round ligaments. [10]
- It has been stated also that endometriosis is also seen in the urinary bladder and uterine cervix. [6]
- It had furthermore been iterated that endometriosis is rarely in remote sites such as the lung, regional lymph nodes or skin. [6]

#### Pathophysiology

The pathophysiology of endometriosis had been summated as follows: [6]

- Retrograde menstruation hypothesis: it had been postulated that endometrial lining cells travel backwards through fallopian tubes during menses to reach the peritoneal cavity, proliferate and cause chronic inflammation with formation of adhesions. [11]
- Coelomic metaplasia hypothesis: it had also been postulated that in endometriosis, metaplastic transformation of coelomic cells lining the pelvic peritoneum do occur. [12]
- Induction hypothesis: It had also been iterated that the development of endometriosis ensues a combination of the first 2 theories. [13]
- It had been iterated that in cases of endometriosis, development of malignant neoplasm occurs in < 1% of cases; 75% of malignant neoplasms arise in ovarian endometriosis [12]

#### Aetiology

The ensuing iteration had been made regarding the aetiology of endometriosis: [6]

- The development of endometriosis is associated with Organochlorine pollutant exposure. [14]

### Clinical features

The clinical manifestations of endometriosis had been summated to include the ensuing: [6]

- Pelvic pain. [15]
- Dyspareunia.
- Dysmenorrhea.
- Infertility.
- Rarely, infection or rupture of an endometriotic cyst with ascites or hemoperitoneum

### Diagnosis

The diagnosis of endometriosis had been summated as follows: [6]

- Laparoscopy is required for definitive diagnosis, even though about 50% laparoscopic biopsy specimens contain microscopic endometriosis. [16]
- Endometriosis within the pelvis is categorized as superficial peritoneal, ovarian and deeply infiltrating endometriosis.

### Radiology description

The radiology-imaging description of endometriosis had been summated as follows: [6]

- Ultrasound scan is stated to be mostly used for the assessment of ovarian endometriotic cysts
- It has been iterated that ultrasound scan of endometriosis typically demonstrates multilocular cysts with septations and hyperechoic mural nodules. [6] [17]

### Prognostic factors

Factors of prognostication associated with endometriosis had been summated as follows: [6]

- In the scenario of endometriosis, the risk of development of malignant neoplasm is estimated at 1% for premenopausal women and up to 2.5% for postmenopausal women
- About 75% of neoplasms complicating endometriosis are stated to arise within the ovary; most common extraovarian site is rectovaginal septum. [6]
  - It has been iterated that there is an increased risk of endometrioid carcinoma followed by clear cell carcinoma [18]
  - Other associated neoplasms noted with endometriosis had been stated to include: seromucinous neoplasms (mainly borderline), endometrioid adenofibromas and borderline neoplasms, adenocarcinomas and endometrial stromal sarcomas. [19]
- It had been stated that women with carcinoma arising within endometriosis tend to be premenopausal, obese and with history of unopposed oestrogens. [20]

- It had been documented that endometriosis associated carcinomas (other than clear cell) tend to be lower grade and stage than similar ovarian carcinoma without associated endometriosis. [21]

### Treatment

The treatment of endometriosis had been stated to include the ensuing: [6]

- Endometriosis associated pain is stated to be treated with non-steroidal anti-inflammatory drugs (NSAIDs), hormonal contraceptives, GnRH analogues and aromatase inhibitors. [15]
- Surgical resection of the endometriosis lesion. [6]

### Gross description

Macroscopy examination features of endometriosis had been summated as follows: [6]

- Ovarian endometriotic cysts (endometriomas) are stated to have fibrotic walls, a smooth lining and dark brown cyst contents (chocolate cyst), often adherent to adjacent organs. [6]
- Polypoid endometriosis is stated to have a polypoid configuration that raises the differential diagnosis of a neoplasm on gross and intraoperative examination. [22]
- Macroscopy examination of specimens of endometriosis had been stated to demonstrate the ensuing: Red, brown, white plaques, sometimes with a gelatinous appearance [6] [15] [23]

### Frozen section description

Frozen section examination features of specimens containing endometriosis had been summated as follows: [6]

- Cytology examination of specimens containing endometriosis is stated to demonstrate presence of endometrial glands or endometrial stroma [23]
  - It has been iterated that sometimes only macrophages and hemosiderin are present or found (and hence the pathologist undertakes the diagnosis as consistent with clinical impression of endometriosis, as other causes are possible)
- Cytology examination of specimens of endometriosis could demonstrated an association of endometriosis with fibrous adhesions. [6]
- Cytology examination of specimens containing endometriosis may be negative for neoplastic features such as glandular complexity. [6]

### Microscopic (histologic) description

The microscopy pathology examination features of specimens of endometriosis had been summated as follows: [6]

- At least 2 of the following 3 features should be demonstrated upon microscopy pathology examination of specimens of endometriosis including: [6]
  - Endometrial type glands
    - Müllerian type epithelium (can be atrophic to cycling endometrium)

- Can show degenerative atypia (enlarged smudgy nuclei) or metaplasia
  - Endometrial type stroma
    - Often contains fine capillary network
    - May undergo smooth muscle metaplasia, fibrosis (longstanding), decidual change
    - May be myxoid (particularly in pregnancy)
    - Stroma may be the only identifiable component (stromal endometriosis)
  - Evidence of chronic haemorrhage ( hemosiderin laden or foamy macrophages)
- Other rare findings that tend to be found upon microscopy pathology examination of specimens of endometriosis include the ensuing: [6]
  - Necrotic pseudoxanthomatous nodules: central necrosis surrounded by histiocytes and outer fibrous zone.
  - Liesegang rings: eosinophilic acellular rings within necrotic tissue. [19]
  - Burnt out endometriosis: this term has been proposed for changes suggestive of endometriosis, such as central necrosis with surrounding fibrosis and pseudoxanthoma cells but lacking confirmatory features as listed above. [6]
  - Atypical endometriosis: this has been reported in 1.7 - 4.4% of endometriotic lesions and is considered the precursor lesion for endometriosis associated carcinomas (clear cell or endometrioid); may be in continuity with these tumours. [6]
    - Includes crowded glands lined by atypical epithelium resembling endometrial atypical hyperplasia; nuclear atypia is typically moderate or severe, with hob-nailing. [24] [25] [26]
    - Endometriosis is stated to be associated with synchronous / subsequent neoplasia in 25% of cases and harbours genomic alterations seen in endometriosis associated tumours. [26]

### Cytology description

Some of the cytology descriptions of endometriosis that had been reported in various structures had been summated as follows: [6]

- Cytology examination features of endometriosis had been reported within peritoneal fluid and fine needle aspiration of scar tissue following gynaecological procedure (for example: in caesarean section specimens) [27]
- Variably sized, 3 dimensional spherules with periphery of polygonal endometrial cells with larger, hyperchromatic nuclei and moderate amount of cytoplasm, often with a centre of stromal cells with hyperchromatic nuclei, scant cytoplasm and indistinct cytoplasmic borders had been demonstrated in

specimens of endometriosis upon cytology examination in some tissues. [28]

- Cytology examination of specimens containing endometriosis may demonstrate admixed hemosiderin laden macrophages. [6]

### Positive stains

It has been stated that immunohistochemistry staining studies of specimens of endometriosis demonstrates positive staining for the ensuing tumour markers: [6]

- **CD10** is documented or identified to be is positive in endometrial stroma. [6]
- **ER, PR, and PAX2** are documented to be often positive within endometrial glands and stroma in cases of endometriosis. [6] [29]

### Molecular / cytogenetics description

Molecular / cytogenetics features of endometriosis had been summated as follows: [6]

- Endometriosis and synchronous carcinoma are stated to share similar genetic alterations including *ARIDIA*, *PTEN* and *PIK3CA*. [6]
- Mutations in *ARIDIA*, a tumour suppressor gene, had been stated to be identified in up to 57% of ovarian endometrioid carcinoma and up to 30% of clear cell carcinoma. [6]
  - Multiple studies had suggested *ARIDIA* mutation occurs at early stage of canceration of endometriosis. [30]
  - It had been iterated that endometriosis occurring distant from *ARIDIA* deficient carcinomas are more likely to retain *ARIDIA* expression. [6]
- Other associated genetic alterations in cases of endometriosis had been documented to include loss of BAF250a, ER and PR and upregulation of hepatocyte nuclear factor - beta and SKP2. [6]
- It had been pointed out that in one study, loss of DNA mismatch repair protein expression was found in 10% of patients with endometriosis associated ovarian carcinoma. [31]

### Differential diagnoses

Differential diagnoses of endometriosis afflicting some organs had been summated as follows: [6]

- **Endocervicosis:**
  - Glandular component is endocervical mucinous type, no endometrial stroma, no haemorrhage. [6]
- **Endosalpingiosis:**
  - Glandular component is tubal (ciliated with peg / intercalated) cells, no endometrial stroma, no haemorrhage. [6]
- **Adenomyosia:** [6]
  - Endometrial glands and stroma are found within the myometrium

- **Endometrioid adenocarcinoma:** [6]
  - Complex glandular growth and cytologic atypia
- **Metastatic carcinoma:**
  - It had been pointed out that the morphology varies by site of origin of the metastatic carcinoma; nevertheless, no endometrial stroma is found in cases of metastatic carcinoma. [6]
  - Other features of neoplasm are noted to be present, including crowded irregular glands, nuclear atypia or elevated mitotic activity. [6]

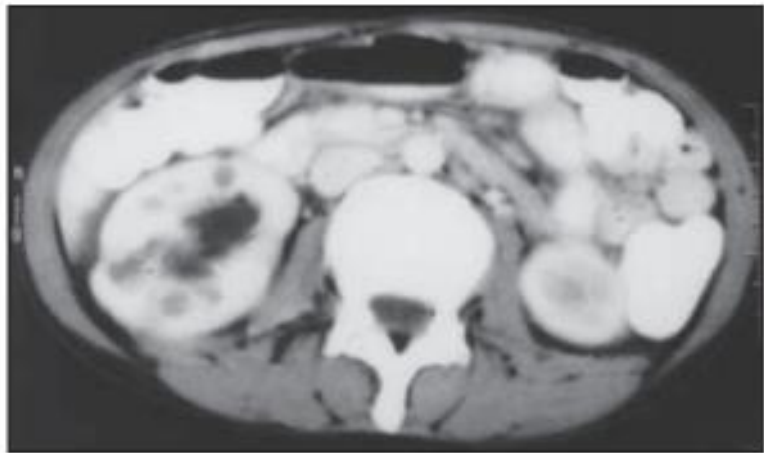
**[B] Miscellaneous Narrations And Discussions From Some Case Reports, Case Series, And Studies Related To Endometriosis Of The Kidney And Urinary Tract Organs**

[1] reported a 38-year-old woman mother of 2 children, who was diagnosed to have thyrotoxicosis 3 months earlier and who was on carbimazole. She manifested with abdominal pain of 2 months duration and she was found to have left ovarian mass that measured 15 cm x 12 cm x 6 cm in size. Prior to her admission she underwent exploratory laparotomy with bilateral salpingo-oophorectomy and she was referred to the urology team for further management with the surgical specimen. She did not have any menstrual irregularities, dysmenorrhea or urinary symptoms. On examination, she was

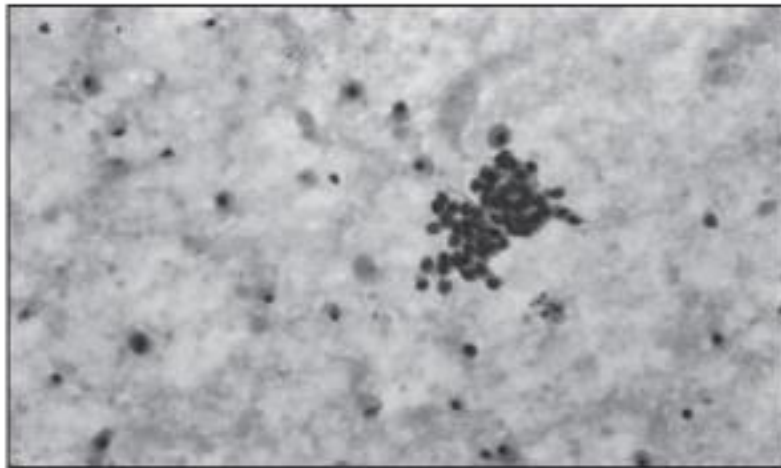
found to be toxic, sick looking, febrile and she had a pulse rate of 102/min, blood pressure 110/70 mm Hg, and body mass index of 12.4 kg/m<sup>2</sup>. She had a grade II goitre without any pressure symptoms. Her systemic examination was noted to be unremarkable except for the finding of a lower midline scar over her abdomen, which was infected with an intra-abdominal swelling. The results of her laboratory test examinations demonstrated a hemoglobin of 11 gm/dl, total leukocyte count of 12,000/mm, creatinine 1.33 mg/dl. Her urine routine examination revealed 12-14 pus cells per high power fields and the urine culture grew *Escherichia coli*. Her T3, T4 and thyrotropin were 2.56 ng/dl [0.6-1.81], 135 ng/dl (45-109), and 0.04 μIU/ml (0.35-5.5). Her thyroid microsomal antibody was positive. A <sup>99m</sup>Tc-scintigraphy of thyroid and whole-body iodine scan demonstrated diffusely increased uptake of tracer in the thyroid bed. A contrast enhanced CT scan of the abdomen was undertaken to look for intra-abdominal collections which demonstrated an enlarged right kidney with a multiple focal-hypodense lesions of varying sizes (5-10 mm) (see Figure 1), and bilateral inflammatory collections in the adnexal area. The right ureter and pelvis-caliceal system were dilated up to the lower end. The surgical specimen of ovary and fine needle aspiration cytology (FNAC) from hypodense areas of kidney showed evidence of endometriosis (Figure 2). She was administered parenteral antibiotics and she underwent pigtail drainage of intraabdominal collection. Subsequently, she received 5 mci of <sup>131</sup>I. During her post-operative 6 weeks follow-up assessment she was found to be euthyroid. An intravenous pyelography was undertaken, and no ureteric obstruction was identified. Danazol of 400gms were orally administered and she was responding very well.

Site	Percentage
Intestine	32
Urinary tract	20
Bladder	49
Ureter	49
Kidney	1
Urethra	1
Lung and pleura	2
Scars	30
Umbilicus	11
Others	2
Inguinal region and thigh	3

**Table 1:** Incidence of extra-genital endometriosis at different sites. Reproduced from [1] Under the Creative Commons Attribution License.



**Figure 1:** Contrast enhanced Ct scan of the abdomen showing multiple hypodense areas in the right kidney. Reproduced from [1] Under the Creative Commons Attribution License.



**Figure 2:** Photomicrograph showing cluster of tubular epithelial cells in a background containing many scattered foamy histiocytes some of which contain hemosiderin. (hematoxylin & eosin x 360). Reproduced from [1] Under the Creative Commons Attribution License.

[1] made the ensuing discussing iterations:

- Extragenital endometriosis is relatively uncommon.
- The lesions may be found within the intestines, urinary tract, abdominal scars, thorax, umbilicus, and the kidneys in that order (see Table 1). [4]
- Genitourinary endometriosis is rare and commonly afflicts the female between 25 years and 40 years.
- It had been stated that urinary bladder is the most site to be involved followed by ureters, kidney, urethra and prostate occurring with a ratio of 40:4:1:1. [5] [32]
- Various postulates had been proposed to explain the occurrence of endometriosis in the extra genital sites.
- Considerable evidence had supported the migratory theory, which suggests that endometrial tissue elements originate within the uterine mucosa and reach an ectopic position by direct invasion, implantation or metastasis. [33]
- More recent evidence had indicated that endometriosis is caused by transplantation of viable endometrial fragments which are shed during menses that are regurgitated through the fallopian tubes due to the influence of prostaglandin mediated uterine contractions. [34]
- Factors that increase the incidence of endometriosis are stated to be those that cause relative uterine outflow obstruction. This postulate could explain the occurrence of renal endometriosis by hematogenous metastatic spread. [35] Nevertheless, no such factors were operative in their reported case.
- Many clinical observers had indicated that endometriosis is oestrogen dependent. Any intervention that decreases oestrogen production typically decreases the extent of endometriosis and oophorectomy is stated to be usually curative. [36]
- Even though, literature review had suggested that renal endometriosis is usually associated with previous pelvic endometriosis, in their case they were almost concurrent and diagnosed coincidentally during the evaluation of postoperative intraabdominal collection.
- The other major postulate to explain their case is the coelomic metaplasia theory. During early embryo genesis, coelomic membrane related cells were disintegrated into the developing kidneys and subsequently stimulated by increased rate of conversion of androgens to oestrogens due to a thyrotoxicosis state.
- In thyrotoxicosis, free oestradiol is decreased and its tissue metabolism is increased, which possibly led to silent disease for a long time in their reported case.
- The common manifestations of endometriosis of the kidney are local pain and rarely cyclical visible haematuria, which is more common with ureteric and urinary bladder endometriosis. It usually comes insidiously and might manifest for many years before the diagnosis established.
- Sometimes the endometriosis lesion may be totally asymptomatic as happened in their case.
- Many cases in the literature were diagnosed upon histopathology examination of kidneys which were removed for presumed renal cell carcinoma. [36] [37]
- Nevertheless, in view of the wider use of FNAC this type of situation would come down in the future.
- Long standing pain from urinary tract and a poor response to common treatments should raise the possibility of endometriosis particularly in women who have had a history of endometriosis, or if the lesions are within the utero-sacral, cardinal ligaments, the ovaries and the pelvic wall. [4]
- Literature has been scant and unhelpful for the treatment of renal endometriosis.
- The choice of therapy depends upon the condition of kidney, the severity of symptoms, the extent of the disease, the age of the patient and whether further pregnancy is planned. [37]
- Their reported patient has already completed her family, and there was no disturbance of kidney function, a total abdominal hysterectomy with bilateral salpingo-oophorectomy had already been undertaken. Hence, she was put on hormonal manipulation with danazol. The lesions regressed slowly.
- During treatment of endometriosis of the kidney, renal function should be closely monitored by clinicians and periodic radiology-imaging should be undertaken to look for regression of lesions. If ovarian inactivation is insufficient, the disease part is usually resected.
- Electro coagulation of smaller lesions is not recommended, as the endometrial tissue grows all the way.

Dutta et al. [1] made the ensuing conclusions:

- Endometriosis of kidney is a rare manifestation of a common disease.
- A high index of suspicion is necessary in order to avoid the undertaking of unnecessary nephrectomy.

Ponticelli et al. [38] made the ensuing iterations:

- Little attention had been paid by the renal literature to endometriosis of the ureter, which is a rare and silent disorder that could eventually emanate in the development of renal failure.
- In endometriosis, the involvement of the ureter could be limited to a single ureter, more often the left one, or both ureters with consequent urine tract obstruction and ureterohydronephrosis.
- In the majority of cases, the ureteric obstruction is caused by endometrial tissue encompassing the ureter (extrinsic ureteral endometriosis).
- In the remaining cases, endometrial cells are located within the ureter (intrinsic ureteral endometriosis).
- Progressive ureteric obstruction of endometriosis could be insidious in onset and could ultimately lead to renal failure if a correct diagnosis is missed.
- The true incidence of renal failure that is caused by endometriosis is completely not known, even though cases had been reported in the literature.
- The diagnosis of endometriosis of the ureter is difficult in view of the fact the disease may be clinically silent or associated with non-specific symptoms.
- Only a high index of suspicion and radiology-image support might help to obtain an early diagnosis. Nevertheless, while radiology renal imaging is useful in the cases of extrinsic endometriosis, the diagnosis of intrinsic endometriosis often requires the undertaking of ureteroscopy or laparoscopy.
- The prognosis of endometriosis of the ureter depends upon the time of diagnosis.
- In too many cases of bilateral obstruction, the patient is referred to the nephrologist in view of an advanced, irreversible renal failure.
- Even though some patients may benefit from progestin or anti-arotamase therapy, in most cases of ureteric endometriosis surgery is needed, laparoscopy surgery being preferred today to laparotomy.

Nezhat et al. [39] made the ensuing iterations:

- Ureteral endometriosis, albeit rare, could be complicated by potential loss of renal function.
- A laparoscopic approach to treatment is based upon the extent of the disease and its localization.
- Endometriosis of the ureter is a serious localization of disease burden which could lead to urinary tract obstruction, with subsequent hydroureter, hydronephrosis, and potential kidney loss.
- Diagnosis of endometriosis of the ureter is elusive and relies heavily upon clinical suspicion as ureteral endometriosis can occur with both minimal and extensive disease.
- Surgical technique to treatment varies, but the goal is to salvage renal function and decrease disease burden.

Nezhat et al. [39] reported 3 cases of endometriosis of the ureter in which there was documentation of renal atrophy and function loss with subsequent workup and surgical intervention. Nezhat et al. [39] stated that the cases had illustrated varying surgical approaches tailored to localization of ureteral endometriosis. All cases were carried out laparoscopically. Nezhat et al. [39] made the ensuing conclusions:

- Endometriosis of the ureter, albeit rare, could be complicated by potential loss of renal function.
- Clinical suspicion and pre-operative assessment might help with diagnosis and enables for a multidisciplinary pre-consultation.
- Laparoscopic surgical approach is based upon the extent of the disease and localization and could be carried out successfully in the hands of a highly experienced laparoscopic surgeon.

Cheng et al. [40] reported a 53-year-old Chinese premenopausal woman, who had manifested with intermittent right flank pain for many years. She had radiology-imaging studies, which demonstrated a contracted non-functioning right kidney and a perinephric abscess. The contracted kidney was adjudged to have resulted from chronic pyelonephritis. The abscess was drained. The patient subsequently underwent a right nephrectomy. Histopathology examination of the nephrectomy specimen revealed endometriosis of renal parenchyma in addition to xanthogranulomatous pyelonephritis and a perinephric abscess. No evidence of endometriosis was identified within the pelvic site. The patient was symptom-free pursuant to the operation. Cheng et al. [40] made the ensuing conclusions:

- Endometriosis is a common benign condition in women of reproductive age which is typified by the presence of endometrial glands and stroma outside the uterine cavity, which afflicts either genital or extragenital sites.
- Involvement of the urinary tract by endometriosis is rare.
- Among the urinary tract endometriosis, only a few cases had been reported to involve the kidney.
- Endometriosis of the kidney is difficult to diagnose; a final diagnosis of endometriosis relies upon the histopathology examination findings.
- Treatment of endometriosis involves hormonal manipulation or a hysterectomy with bilateral salpingo-oophorectomy.
- Whether a is nephrectomy required depends upon the level of renal function. #
- Even though extremely rare, renal endometriosis should be part of the differential diagnostic spectrum when a contracted, non-functioning kidney is found.
- Early diagnosis might have prevented the undertaking of an unnecessary nephrectomy in cases of uncomplicated renal endometriosis.

Horn et al. [41] stated the following:

- Urinary tract endometriosis is rare and occurs in about 1% of all endometriotic lesions.
- About 30% of patients suffer from reduced kidney function at the time of diagnosis.

Horn et al. [41] reported a 49-year-old woman, who had manifested with a history of abdominal hysterectomy without adnexae because of uterus myomatosis without any signs of endometriosis 6 years earlier. She six years subsequently complained of dysuria and intermittent left loin pain. She had ultrasound scan and retrograde pyelography which demonstrated incomplete ureteric obstruction and her scintigraphy demonstrated a partial loss of kidney function. Intraoperatively frozen section histology examination and final histopathology examination demonstrated a tumorlike intrinsic form of ureteral endometriosis engulfing the left ureter. The patient was treated with uretero-ureterostomy and danazole for preventing recurrence. She was well 28 months post-operatively. Horn et al. [41] made the ensuing conclusion:

- In the extrinsic form (of about 75% of all cases), endometriosis of the ureter is localised to the adventitia or surrounding connective tissue of the ureter, whereas the intrinsic form of ureteral endometriosis is very rare and more often needs aggressive surgery.

Chen et al. [42] stated that endometriosis, mainly occurs in female pelvic organs and that endometriosis in the kidney is extremely rare. Chen et al. [42] reported a case of a 19-year-old girl who had occasional mild abdominal pain that was associated with an ectopic left kidney. She had SPECT-CT scan which showed no abnormal radioactive distribution in the left pelvis, indicating loss of function of the ectopic kidney. Laparoscopic left ectopic kidney resection was subsequently undertaken. Histopathology examination of the excised specimen revealed endometriosis of the ectopic left kidney. Chen et al. [42] concluded that:

- In female patients with clinical manifestations of abdominal pain and visible haematuria, the possibility of renal endometriosis should be considered.

Giambelluca et al. [43] made the ensuing iterations:

- Endometriosis is a common gynaecological disorder typified by ectopic endometrial tissue growth outside the uterine cavity.
- Even though usually occurring within pelvic organs, endometrial lesions might involve the urinary tract.
- Endometriosis of the kidney is extremely rare and it has only occasionally been reported in the past.

Giambelluca et al. [43] reported two cases of patients with renal cystic lesions, which were incidentally found by radiology imaging techniques during oncologic follow-up for gastric sarcoma and melanoma, which was initially misinterpreted as complicated haemorrhagic cysts and then histologically characterized as renal localizations of extragenital endometriosis. Giambelluca et al. [43] made the ensuing discussions and conclusions:

- Their cases were two examples of asymptomatic patients with history of ovarian endometriosis and incidental detection of renal endometriotic lesions, subsequently histopathological examined.
- These patients do not need any therapy for renal lesions being asymptomatic and unchanged on the subsequent imaging examinations.
- From literature data most of the previously reported examples of endometriosis of kidney were found in symptomatic patients.
- Renal endometriosis is a rare entity which may be asymptomatic or clinically controversial and the diagnosis is possible only in presence of an appropriate clinicaassessment.

- CECT and MR might be helpful in staging the disease process and for differential diagnosis from other blood containing lesions, even though definitive diagnosis requires histology examination confirmation by identifying endometrial glands and stroma within the renal lesions.

Katsikasos et al. [44] stated that renal endometriosis is an uncommon disorder of cases of urinary tract endometriosis. Katsikasos et al. [44] reported a 42-year-old woman, who presented at their outpatient department with an incidental painless mass upon her left hypoplastic kidney which was demonstrated on an abdominal ultrasound scan. She had abdominal and pelvic examinations which revealed no abnormal findings. She had a computed tomography (CT) scan which showed an anterolateral slightly enhanced left renal mass which measured 1.2 cm in diameter. In addition, the CT scan did not reveal any evidence of abdominal or thoracic metastasis. Katsikasos et al. [44] stated also that there were a few case reports in the literature of tumours in specimens from patients who had undergone nephrectomy for hypoplastic kidneys, but discriminating between benign and malignant masses is difficult unless a nephrectomy is undertaken. Given the radiological findings and the impaired function of the hypoplastic kidney, laparoscopic radical nephrectomy was recommended. The procedure was undertaken under general anaesthesia without intraoperative or postoperative complications. Microscopy examination of the excised specimen revealed many findings that were consistent with a diagnosis of renal endometriosis. The patient had no symptoms during her last follow-up visit. Katsikasos et al. [44] concluded that:

- The case had highlighted that renal endometriosis can simulate renal cell carcinoma and awareness of this entity should be raised, as it could be asymptomatic, especially when located in a hypoplastic kidney.

Huang et al. [45] undertook a study to determine the risk of chronic kidney disease (CKD) among women with endometriosis in Taiwan. Huang et al. [45] undertook a retrospective cohort study using the National Health Insurance Research Database of Taiwan. Huang et al. [45] selected a total of 27,973 women with a diagnosis of endometriosis and 27,973 multivariable-matched controls (1:1) from 2000 to 2010. Huang et al. [45] reported that Cox regression and computed hazard ratios (HR) with 95% confidence intervals (95% CI) were utilised to determine the risk of CKD among women with endometriosis. Huang et al. [45] summated the results as follows:

- The incidence rates (IR, per 10,000 person-years) of CKD among women with and without endometriosis were 4.64 and 7.01, respectively, with a significantly decreased risk of CKD (crude HR 0.65, 95% CI 0.53–0.81; adjusted HR 0.69, 95% CI 0.56–0.86) among women with endometriosis.
- The IR of CKD progressively had increased with age, but the trend of lower CKD risk among women with endometriosis was found to be consistent.
- Nevertheless, the lower risk of CKD in women with endometriosis was no longer statistically significant after adjusting for menopausal status (adjusted HR 0.85, 95% CI 0.65–1.10).

Huang et al. [45] made the ensuing conclusions:

- The results had suggested that endometriosis is inversely associated with CKD, but this effect was mediated by menopause.
- The possible mechanism of this association is worthy of further evaluation.



Gagnon et al. [46] reported a 27-year-old woman, who was known to have a solitary left kidney since the age of 17 years. In her early 20s she was investigated for recurrent lower abdominal pain that was related to her menstrual periods. At the age of 25 years (in 1997), her pain within the right inguinal area was explored surgically, and endometriosis within the proximity of the round ligament was found and excised. Her cyclic pelvic pain was investigated further and a laparoscopy demonstrated endometriosis within the Douglas pouch. The patient was also known to have a bicornuate uterus, which was considered to be a risk factor for endometriosis. While waiting for definitive surgery of pelvic endometriosis (in December 1997), she manifested with recurrent episodes of fever, anorexia, nausea and fatigue accompanied by pelvic pain beginning in the middle of her menstrual periods and lasting for a few days afterwards. She had noted progressive polyuria and nocturia. She came to medical attention in April 1998, during a more severe cyclic episode in which she manifested with vomiting and headache. She was found to be severely hypertensive (blood pressure 200/120) with an elevated serum creatinine at 201  $\mu\text{mol/l}$  (baseline value of 89  $\mu\text{mol/l}$  in 1989). An ultrasound was undertaken which showed hydronephrosis of the solitary left kidney with hydroureter. A retrograde pyelogram was undertaken which demonstrated severe obstruction of the distal ureter of the solitary kidney. A double J catheter was advanced with difficulty into the left ureter through the tight distal stenosis. Her clinical symptoms corrected readily together with improvement in her serum creatinine level.

Alhindawi et al. [47] made the ensuing iterations:

- Ureteral endometriosis commonly manifests with non-specific symptoms or no symptoms.
- Diagnostic challenges are multifactorial but they essentially are caused by diagnostic delay due to the silent nature of the disease.
- Management of endometriosis of the ureter requires a multidisciplinary approach to optimise the outcome.

Alhindawi et al. [47] reported a 29-year-old woman, who presented with severe deep infiltrating endometriosis resulting in bilateral hydronephrosis and loss of left kidney function. She underwent laparoscopic excision of deep infiltrating endometriosis, ureterolysis, bowel resection and colostomy formation. Eventually the left non-functional kidney required nephrectomy. Alhindawi et al. [47] made the ensuing conclusions:

- The presence of posterior deep infiltrating endometriosis with uterosacral involvement should increase clinical suspicion of ureteral endometriosis and trigger targeted investigations.
- The best outcome is achieved by the individualisation of patient's care.

Carmignani et al. [48] assessed whether routine renal ultrasound scan may be recommended in all patients with pelvic endometriosis, in order to avoid silent ureteral involvement of the disease. Carmignani et al. [48] undertook a retrospective descriptive study on seven hundred and fifty patients with a primary diagnosis of endometriosis, between January 2005 and July 2007. Routine urinary ultrasound; recording of patient history, signs, and symptoms; gynecologic examination; blood and urinary analyses; magnetic resonance imaging; spiral multi-slice computerized tomography, were undertaken. Carmignani et al. [48] summated the results as follows:

- Twenty-three patients (3%) of all 750 patients with endometriosis had associated ureterohydronephrosis which were diagnosed at renal ultrasound.
- Symptoms secondary to ureteric and renal involvement were present in 10 patients (43.5%); 6 patients reported lumbar pain (26.1%) and 4 patients (17.4%) had renal colic.

Carmignani et al. [48] made the ensuing conclusion(s):

- In their study, the high number (56.5%) of asymptomatic ureteral involvement in patients with known pelvic endometriosis seemed to warrant the need for further investigations regarding the possibility to avoid the high percentage of silent renal losses.
- Unfortunately, there appeared to be no specific risk factor to allow for early suspicion nor a validated preventive diagnostic and therapeutic program.
- It had remained to be evaluated whether urinary ultrasound ensures a beneficial cost-benefit ratio if undertaken on a routine basis.

Arrieta Bretón et al. [49] reported on the impact that urinary tract endometriosis may have on renal function. They stated that ureteral endometriosis is an uncommon and a silent cause of renal injury as well as that it is therefore very important to be highly suspicious in order to be able to make an early diagnosis and thus prevent renal failure. Arrieta Bretón et al. [49] reported on cases documenting on the management and outcome of three cases of premenopausal women with deep endometriosis affecting the ureter, associated with secondary unilateral complete loss of renal function. Arrieta Bretón et al. [49] summated the results with conclusions as follows:

- Ureteral involvement by endometriosis is a rare and often silent disease which is capable of producing significant morbidity, as it could lead to the development of hydronephrosis and ultimately to renal failure.
- Due to the lack of specific symptoms and the limitations of radiology-imaging methods, a high index of suspicion is necessary in order to obtain an early diagnosis.
- On diagnosis of deep infiltrating endometriosis, urinary tract ultrasound scan is a screening tool to identify ureterohydronephrosis due to ureteral obstruction.
- MRI scan is of value to map the extent of disease.
- Surgery is the therapy of choice to remove endometriotic lesions and relieve ureteral obstruction if the kidney is still functional, or to undertake a nephrectomy if there is a complete loss of renal function.

Langebrette and Qvigstad [50] made the ensuing iterations:

- Ureteral endometriosis is associated with deep endometriosis and is relatively uncommon.
- In some patients, progressive obstruction of the lower part of the ureter might develop, with silent loss of kidney function as a consequence.

Langebrette and Qvigstad [50] reported on three patients with loss of renal function, in whom different pathogenic mechanisms probably were the decisive cause. Langebrette and Qvigstad [50] stated the following:

- Failure to diagnose deep endometriosis with ureteric involvement, misinterpretation of hydroureter at magnetic resonance imaging and lack of typical symptoms could all be reasons for development of loss of renal function.
- With only one functional kidney, these patients should be followed-up closely with the undertaking of kidney function tests and ultrasound scan, and in certain cases also by magnetic resonance imaging scan or renal scintigraphy.

Yohannes [51] undertook a comprehensive literature review of reports on the diagnosis and management of ureteral endometriosis was performed using MEDLINE. Yohannes [51] summated the results as follows:

- Ureteral endometriosis is a rare disease.
- Most cases manifest with silent obstruction, as opposed to cyclical haematuria.
- The diagnosis of endometriosis of the ureter requires a high index of suspicion.
- A variety of diagnostic tests could help identify the extent of disease and the degree of renal function on the side of ureteric involvement.

Yohannes [51] made the ensuing conclusions:

- Ureteral endometriosis could be treated with hormones or surgical intervention.
- While surgery is reserved for hormone refractory cases and obstruction associated with extensive scarring, the majority of cases could be managed with hormones only.
- A combination of hormones and surgery is also effective.
- Surveillance for obstructive uropathy with periodic non-invasive monitoring of renal function is currently recommended for all patients with endometriosis.

Pérez et al. [52] undertook a retrospective analysis of 12 cases of urinary tract endometriosis diagnosed from 1993 to 2008. Pérez et al. [52] summated the results as follows:

- The mean patient age was 37.75 years.
- Out of the 12 patients, 5 had urinary bladder involvement and 7 had ureteric involvement, 2 bilateral, 2 left, and 3 right.
- In those with urinary bladder endometriosis, the diagnosis was made by cystoscopy and biopsy in 4 patients.
- The treatment consisted of laparoscopic hysterectomy and partial cystectomy in 1 patient and exploratory laparotomy, trans-vesical resection, and transurethral resection of the bladder in 3 patients.
- One of the patients who underwent transurethral resection of the urinary bladder lesion experienced 2 relapses. The first relapse was treated with transurethral resection of the urinary bladder lesion and the second with laparoscopic partial cystectomy.
- In the patients with ureteric endometriosis, the diagnosis was mainly established by magnetic resonance imaging scan.
- The treatment consisted of ureteroneocystostomy in 5 patients (bilateral in 1) and laparoscopic ureterolysis in 2, with later ureteric lesion resection and end-to-end anastomosis in 1 of them.
- The patient who underwent bilateral ureteroneocystostomy finally required right auto-transplantation in view of early ureteral relapses.

Pérez et al. [52] made the ensuing conclusions:

- Urinary tract endometriosis is an uncommon pathology finding.
- Surgery is the treatment of choice.

- They believe partial cystectomy should be considered as an initial option in selected cases, depending upon the extent and location of lesions.
- For cases of endometriosis of the ureter, the initial technique depends upon the location and depth of the lesion.

Knabben et al. [53] analysed the prevalence of urinary tract endometriosis (UTE) in patients with deep infiltrating endometriosis (DIE) in order to define potential criteria for preoperative workup. Knabben et al. [53] undertook a retrospective study of six hundred and ninety-seven patients with endometriosis who underwent excision of all endometriotic lesions. Knabben et al. [53] undertook a correlation of preoperative features and intraoperative findings in patients who had UTE. Knabben et al. [53] summated the result(s) as follows:

- Out of 213 patients presenting DIE, 52.6% had suffered from UTE.
- In patients who had ureteric endometriosis, the manifesting symptoms were not specific.
- Among the patients with urinary bladder endometriosis, 68.8% had complained of urinary symptoms compared to 7.9% in the group of patients without UTE.
- In patients who had rectovaginal endometriosis, the probability of ureterolysis demonstrated a linear correlation with the size of the nodule.
- They found that 3 cm in diameter provided a specific cutoff value for the likelihood of ureteric involvement.

Knabben et al. [53] made the ensuing conclusion:

- The prevalence of UTE had often been underestimated.
- Pre-operative questioning is important in the search for urinary bladder endometriosis.
- The size of the nodule is one of the few reliable criteria in preoperative assessment that can suggest ureteric involvement.
- They had proposed a classification of endometriosis of ureter that would allow the standardization of terminology and help to compare the outcome of different surgical treatment in randomized studies.

Badri et al. [54] made the ensuing iterations:

- Endometriosis is a multi-factorial benign disorder which is typified by the abnormal presence of endometrial tissue in an extra-endometrial site.
- Even though extra-pelvic endometriosis is not common, symptomatic involvement of the kidney is very rare.
- This benign disease could simulate many urological processes, but because of its scarcity in clinical practice, it is seldom considered in the differential diagnosis.

Badri et al. [54] reported the case of a 45-year-old woman with flank pain and haematuria, who was found to have a left kidney mass on cross-sectional imaging. After robotic partial nephrectomy was undertaken, pathology analysis of the specimen revealed an endometrial implant within the renal parenchyma. Badri et al. [54] concluded that:

- Their reported case of renal endometriosis had highlighted how this benign disease process could simulate many more sinister urologic processes.

Gabriel et al. [55] reported on the prevalence, surgical management, and outcome of urinary tract endometriosis (UTE) in a cohort of 221 patients who had undergone laparoscopic surgery for severe endometriosis. They stated that UTE can cause significant morbidity, such as silent kidney or progressive renal function loss and that its frequency is underestimated and data on laparoscopic management are scarce. Gabriel et al. [55] undertook a retrospective study between 2007 and 2010, of 43 patients who were eligible for their single-centre study. The inclusion criterion was the presence of UTE (for example urinary bladder and/or ureteric endometriosis). All patients were operated laparoscopically. Gabriel et al. [55] summated the results as follows:

- The prevalence of UTE was 19.5% (43/221).
- There was no correlation found between urinary bladder and ureteral endometriosis ( $P > .05$ ).
- Endometriosis of ureter was associated with patient's age ( $P < .01$ ).
- Patients who had urinary bladder, but not ureteral, involvement complained more frequently about dysuria, visible haematuria, and urinary tract infections.
- Intraoperative and magnetic resonance imaging (MRI) scan findings demonstrated a moderate to good correlation.
- UTE was not associated with rectovaginal or bowel endometriosis, but rather with the involvement of the uterosacral ligaments ( $P < .01$ ).
- Twenty-two patients with endometriosis of the urinary bladder were treated by mucosal skinning and 11 patients underwent partial cystectomy.
- Superficial ureteral excision was undertaken in 4 patients, whereas resection with ureteroureterostomy was undertaken in 9 patients.
- There was no difference regarding the intra- and postoperative complications in patients with or without UTE.

Gabriel et al. [55] made the ensuing conclusions:

- In severe pelvic endometriosis, involvement of the urinary tract is quite common.
- Laparoscopic management is feasible and safe.
- In view of the lack of specific symptoms, the pre-operative diagnosis of ureteral endometriosis still has remained a challenge.
- Pelvic MRI scan represents a useful preoperative diagnostic tool.

Muthuppalaniappan et al. [56] reported a case of a 30-year-old female, who had a background history of SLE with a silent progressive kidney injury due to an obstructive uropathy secondary to bilateral intrinsic UE and severe loss of her left kidney function that was treated with ureteric stenting. She subsequently underwent bilateral re-implantation of her ureters as a definitive treatment plan as she had expressed a desire to conceive.

Muthuppalaniappan et al. [56] made the ensuing discussing iterations:

- Progressive renal injury as a result of UE had been reported in the past; nevertheless, its true incidence is not known.
- The time of diagnosis is crucial as it does reflect renal prognosis.
- They had outlined in their article the clinical implications from the renal perspective of the disease considering the relevant health problem UE can impose to women.
- Their paper had discussed the emerging evidence of an association between SLE and endometriosis which had remained poorly understood.

Muthuppalaniappan et al. [56] made the ensuing conclusions:

- A high index of suspicion is required to diagnose UE as the disease occurs insidiously with non-specific manifesting symptoms leading to a silent obstructive uropathy.
- If the diagnosis is missed it could ultimately lead to irreversible kidney dysfunction and mortality.
- They had suggested that patients with endometriosis especially UE should be followed up regularly with renal function testing and imaging.
- Any health professionals who are dealing with patients suffering from SLE should consider appropriate investigations and referral if any symptom that indicates endometriosis is reported.

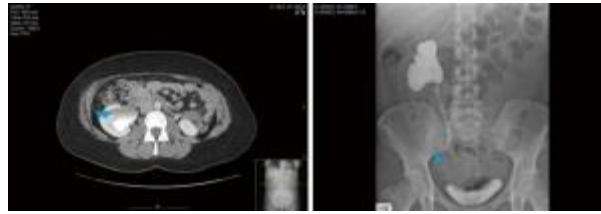
Vrettos et al. [57] made the ensuing iterations:

- Endometriosis is stated to be a common disorder which afflicts 5% to 10% of women of reproductive age, for which the gold standard investigation for the diagnosis is laparoscopy and biopsy with histological confirmation. [58] [59]
- Urinary tract endometriosis occurs in about 1% of women with pelvic endometriosis. [60]
- Endometriosis involves the ureters, it could manifest with renal colic and can cause hydronephrosis and renal complications due to obstruction, mainly in women of child-bearing age.
- The manifesting symptoms could be non-specific.
- Delayed diagnosis could lead to the development of kidney failure due to silent obstruction of the ureter. [61]

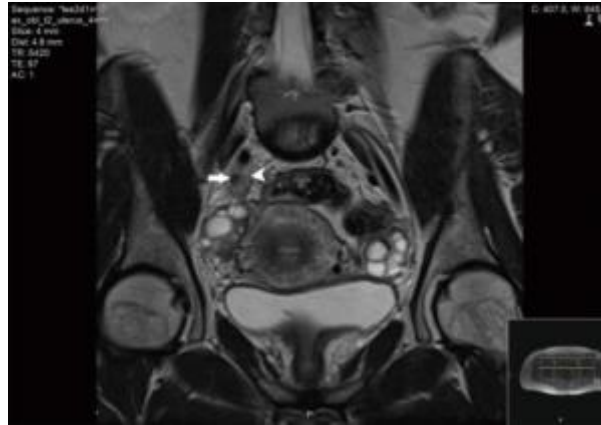
[57] reported a case of a 43-year-old lady who manifested with recurrent episodes of right-sided colicky abdominal pain. She manifested with severe, right-sided colicky abdominal and right loin pain which radiated to the right groin. She reported similar episodes of pain previously, but no clear diagnosis had been established. Her primary care physician had treated her conservatively for possible kidney stones, even though there was no radiology-image evidence to support that. Upon examination, she was found to be afebrile and her vital signs were stable. Her blood results demonstrated a mild elevation in her urea and creatinine levels. She had a computed tomography scan of the kidneys-ureter-bladder (CT KUB), which showed a moderate degree of right sided hydronephrosis but no stone was identified (see figure 3). An intravenous urogram (IVU) was undertaken which demonstrated marked distension of the right pelvic calyceal system and narrowing of the right distal ureter (see figure 3). The patient then subsequently had a magnetic resonance imaging (MRI) scan which demonstrated abnormal soft tissue thickening within the right adnexal region, but no clear cause of the ureteric obstruction was demonstrated (see figure 4). She then underwent laparoscopy to ascertain the nature of the pathology and to provide tissue diagnosis. The pathology findings

demonstrated elements of endometrial tissue which had encased the distal ureter. In view of the proximity of the ureteric stenosis to the ureterovesical junction, the patient was treated by means of an open ureterocystoneostomy. She had an uncomplicated course and her pain resolved after the operation.

She did not experience any further episodes of pain. She had been followed up as an outpatient regularly with monitoring of her renal function, which had remained normal and stable.



**Figure 3:** Computed tomography scan of the kidneys-ureter-bladder (CT KUB) demonstrating right sided hydronephrosis (arrow). Intravenous urogram (IVU) showing narrowing of the right distal ureter (arrowhead). Reproduced from [57] Under the Creative Commons Attribution License.



**Figure 4:** Magnetic resonance imaging (MRI) scan of the pelvis showing abnormal tissue (arrowhead) which encases the right distal ureter (arrow). Reproduced from: [57] Under the Creative Commons Attribution License.

[57] made the ensuing discussions and conclusions:

- Their case had highlighted an uncommon yet important cause of ureteric stricture which could even lead to loss of kidney function. [62]
- The diagnosis relies heavily upon clinical suspicion and definitive treatment might be difficult to be achieved.
- Magnetic resonance imaging scan is a useful pre-operative tool for the diagnosis and assessment of ureteral endometriosis. [63]
- It is important that this underdiagnosed condition, which might ultimately lead to renal failure, be diagnosed as early as possible.
- Then every effort needs to be made in order to restore and preserve kidney function. [64]
- In patients who have hydronephrosis and the localization of the ureteric stenosis close to the vesicoureteral junction, the appropriate procedure is a ureterocystoneostomy, which is typically undertaken through an open technique. [65]
- The laparoscopic procedure had also been successful in the treatment of distal ureteric stenosis. [66]

[67] made the ensuing iterations:

- Endometriosis of the kidney is a rare disease for which the mechanisms of pathogenesis are still unclear.

- In view of this, early diagnosis and an appropriate treatment are often delayed because of the tendency to be misdiagnosed as a renal tumour.
- In October 2013 they undertook a radical nephrectomy for a 37-year-old woman with renal endometriosis who was preoperatively misdiagnosed as having a right renal tumour.
- Avoiding the misdiagnosis of renal endometriosis entails a detailed case history taking, especially regarding whether the cyclicity of lumbodorsal pain and haematuria correlates with patients' menstrual cycles.
- Radiology imaging examinations are commonly helpful for localization, whereas relieving symptoms with medicaments to create a hypoestrogenic state is useful for clinical diagnosis.
- Nevertheless, a final diagnosis for renal endometriosis still should depend upon histopathologic examination.

[68] made the ensuing iterations:

- Ureteral endometriosis is estimated to occur in about 0.08% to 1% of patients with endometriosis.
- The serious condition, may lead silently to obstruction of the urinary tract leading to hydronephrosis, hydroureter and potential loss of kidney function.

- Endometriosis of the ureter is often associated with endometriomas, deeply infiltrating endometriosis, and the involvement of uterosacral ligaments.
- Diagnosis of endometriosis is often challenging due to the silent nature of the disease and the presence of non-specific or no symptoms.

Nagar et al. [68] reported a 30 years old healthy woman, who was admitted due to abdominal pain lasting for 5 days without fever. She complained of dysmenorrhea but no other gynaecological, urinary or digestive symptoms. She had trans vaginal + abdominal ultrasound (US) of a left ovarian unilocular cyst that measured 85\*83\*123mm with "ground glass" content, which was suspected for endometrioma. Severe hydronephrosis of left kidney with dilated calyx and cortical thinning, pelvic tubular structure 30\*18 with clear fluid was suspected for dilated left hydroureter. Under radiology-imaging limitations there were no signs of DIE CT UROGRAPHY was undertaken which confirmed the urinary system findings. Her laboratory test serum creatinine was 0.79, the results of her electrolytes were normal. Surgery (laparoscopy) drainage of 10cm left endometrioma, left salpingectomy due to LT hydrosalpinx, removal of 4cm deep infiltrating endometriotic nodule that involved the left ureter, left uterine artery and left infundibulo-pelvic ligament was and left were nephroureterectomy undertaken.

[68] made the ensuing conclusions:

- Non-specific symptoms and incorrect diagnosis of ureteral endometriosis could lead to renal damage as a result of prolonged hydronephrosis.
- In view of this, in routine targeted ultrasound scan for endometriosis, radiology-imaging of the kidneys should form an integral part of assessment.
- Physicians should suspect endometriosis of the ureter in reproductive age women with unilateral or bilateral distal ureteral obstruction of uncertain cause.
- A high index of suspicion and utilisation of imaging modalities enable earlier diagnosis, preservation of renal function, and improved prognosis.

[69] presented data from 18 cases of ureteral endometriosis. They undertook Prospective clinical study of four hundred and five patients with severe dysmenorrhea or deep dyspareunia due to a rectovaginal endometriotic (adenomyotic) nodule. The patients were prospectively evaluated using intravenous pyelography. All of the patients underwent laparoscopic surgery to remove rectovaginal adenomyosis and ureterolysis. The main outcome measure included presurgical and postsurgical evaluation and histological analysis.[69] summated the result(s) as follows:

- Preoperative intravenous pyelography revealed ureteral stenosis with ureterohydronephrosis in 18 patients (4.4%).
- A significantly higher prevalence (11.2%) was observed in nodules  $\geq 3$  cm in diameter.
- Five women (20%) were found to have kidney parenchymal function, which ranged from 18% to 42%.
- Laparoscopic ureterolysis was undertaken in 16 women; 2 women underwent ureteral resection and uretero-ureterostomy.

- A significant postoperative decrease in ureterohydronephrosis was identified noted in all patients; nevertheless, renal function improved only slightly.

They made the ensuing conclusion(s):

- Ureteral endometriosis was found in 4.4% of patients with rectovaginal endometriotic (adenomyotic) nodules.
- Ureterolysis and removal of associated adenomyotic lesions was sufficient therapy in most patients; two required resections of the ureteric stenotic segment.
- Intravenous pyelography should be performed in all women with rectovaginal nodules  $\geq 3$  cm to prevent non-reversible loss of renal function.

[70] reported a 29-year-old woman, who manifested with unilateral loin pain because of severely hydro-nephrotic kidney due to deposits of pelvic endometriosis. Double J-stent was inserted beyond the obstruction and she was commenced on hormone therapy. The stent was removed after three months when her back pressure changes had resolved. Gupta et al. [70] concluded that the case was presented along with a short relevant discussion, due to rarity of ureteral involvement by endometriosis.

[71] reported a 42-year-old woman, who was referred to their hospital because of abdominal fullness and a large abdominal mass and other symptoms. She had computed tomography (CT) scan and retrograde pyelography (RP) which revealed left hydronephrosis and a filling defect in the left lower ureter. Based on the diagnoses of endometriosis of bilateral ovaries, uterine myoma and a left ureteral tumour, abdominal total hysterectomy, right salpingo-oophorectomy and partial ureterectomy were undertaken. Pathologically, within the uterus, both leiomyoma and adenomyosis, and endometriosis of the right ovary and ureter were diagnosed. Medication with buserelin acetate was commenced.

[72] stated that deep endometriosis (DE) could be more aggressive than other-types of endometrioses, and might even lead to irreversible severe complications such as complete unilateral loss of kidney function. Martinez-Zamora et al. [72] described the clinical and radiology-image characteristics of DE patients who were diagnosed with irreversible unilateral loss of renal function due to unilateral ureteral stenosis and they evaluated risk factors for developing this loss. The study of Martinez-Zamora et al. [72] was a retrospective cohort study, which included 436 patients who underwent laparoscopic DE surgery. Martinez-Zamora et al. [72] evaluated two groups of patients according to preserved (Non-Renal Loss Group; n = 421) or irreversible unilateral damaged renal function (Renal Loss Group; n = 15). They collected pre-operative epidemiologic variables, clinical characteristics, radiologic findings and surgical treatments of all the patients. They found that the Renal Loss Group had a higher infertility rate and a higher proportion of asymptomatic patients. The following radiology image variables showed statistically significant differences between the two groups: mean endometrioma diameter, the presence of intestinal DE and negative sliding sign. Multivariate analysis showed that infertility, being asymptomatic, having intestinal DE or torus uterinus/uterosacral ligament DE and a negative sliding sign significantly increased the risk of loss of renal function. Martinez-Zamora et al. [72] concluded that:

- Among patients with these clinical and/or radiological variables, severe urinary tract obstruction should be specifically excluded.

[73] reported a patient who underwent laparoscopic endometriosis resection with right ureterolysis, left nephrectomy, left salpingo-oophorectomy, lysis of adhesions. Nephrectomy and contralateral

ureterolysis and dissection of pelvic spaces for successful resection of endometriosis and maintenance of solitary ureter patency was undertaken in order to preserve remaining kidney function. Colussi et al. [73] made the ensuing conclusions:

- Renal function and structure should be regularly evaluated in patients who are afflicted by deep infiltrating endometriosis.
- Surgical intervention, with complete resection of endometriosis, is the optimal approach for prevention of recurrence of ureteral endometriosis.

[74] made the ensuing iterations:

- Endometriosis is a benign condition afflicting up to 10% of women at reproductive age.
- The urinary tract is affected in 0.3% to 12.0% of women with endometriosis and in 19.0% to 53.0% of women with deep infiltrating endometriosis.
- The urinary bladder is the most commonly affected organ in the urinary tract.
- Urinary bladder endometriosis is defined by the presence of endometriosis lesions within the detrusor muscle, with partial or complete thickness involvement.

[74] undertook a retrospective study. The study analysed surgical reports of 11,714 patients who underwent endometriosis laparoscopy, and included only 42 patients with urinary bladder endometriosis. Piriyeve et al. [74] summated the results as follows:

- They found that 0.35% of patients with endometriosis had bladder endometriosis.
- In total, 29 patients underwent telephone phone follow-up.
- In total, 26 patients (90%) had reported a general improvement in their symptoms (for example, improving the dysmenorrhea, lower abdominal pain), with a 100% improvement in their dysuria.
- Only two patients (7%) reported no change in their symptoms (dysmenorrhea and dyspareunia).

[74] made the ensuing conclusions:

- Gynaecologists can undertake laparoscopic surgical treatment of urinary bladder endometriosis in most cases.
- If ureteroneocystostomy is required or the localization of the endometriosis nodule is unfavourable, an intervention by an interdisciplinary team is recommended.
- Both laparoscopic partial bladder resection and shaving could be considered to be effective methods with low complication risk.
- This surgical approach requires excellent laparoscopic skills.

[75] made the ensuing iterations:

- Abdominal wall endometriosis (AWE) consists of endometrial tissue between the peritoneum and the abdominal wall.
- The established treatment involves amenorrheic medicaments which are not always successful and tolerated, or invasive surgery.

- In this scenario, minimally invasive techniques such as cryoablation are a potential option.
- They had undertaken a study, with the aim of evaluating the efficacy of percutaneous cryoablation in reducing pain scores of AWE patients and they had analysed their satisfaction with the procedure and its related adverse events.

[75] systematically searched MEDLINE, EMBASE, and Cochrane's databases for studies that employed percutaneous cryoablation therapy for AWE and reported any of the outcomes of interest. The primary outcome was the reduction in the visual analogue scale (VAS) score after treatment. R Software was used for the statistical analysis. Heterogeneity was assessed using I statistics. They assessed the risk of bias in non-randomized studies of interventions framework for potential bias in each selected study. Kaça do Carmo et al. [75] summated the results as follows:

- They included 4 studies, containing 126 patients.
- All articles were retrospective studies.
- The difference between the VAS scores before and after treatment was on average 5.97 points (95% CI 5.42-6.52;  $P < .01$ ;  $I^2 = 0\%$ ).
- The pooled satisfaction rate among patients in the selected studies was 93.1% (95% CI 88.66-97.34;  $P = .51$ ;  $I^2 = 0\%$ ).
- The pooled prevalence of adverse events was only 5.48% (95% CI 1.71-11.20;  $P = .58$ ;  $I^2 = 0\%$ ).
- Bias analysis revealed an overall moderate risk in all included articles.

[75] made the ensuing conclusions and declaration of advances in knowledge:

- Their study had demonstrated that cryoablation could reduce pain complaints in patients, while presenting a low incidence rate of adverse effects.
- Randomized clinical trials with a larger number of patients are needed for greater conclusions.
- AWE affects about 3.5% of women.
- The standard treatment is invasive surgery.
- This meta-analysis had shown that cryoablation could effectively reduce pain scores while presenting a low rate of adverse effects.
- Cryoablation is a feasible treatment for AWE, furthermore enabling shorter hospital stays and few complications for the patients.

[76] undertook a study to evaluate the efficacy of percutaneous cryoablation in the treatment of abdominal wall endometriosis (AWE) nodules. Bachour et al. [76] retrospectively included thirty-eight women, who were treated for symptomatic AWE nodules with percutaneous cryoablation under ultrasound and computed tomography (CT) guidance between May 2020 and July 2023. Pain was estimated using visual analog scale (VAS) and assessed at baseline, three months, six months, and 12 months after percutaneous cryoablation. Baseline VAS score, volume of AWE nodule and magnetic resonance imaging (MRI) features of AWE nodules were compared to those obtained after percutaneous cryoablation. Major complications, if any, were noted. Bachour et al. [76] summated the results as follows:

- Thirty-eight women who had a median age of 35.5 years (interquartile range [IQR]: 32, 39; range: 24–48 years) and a total of 60 AWE nodules were treated.
- Percutaneous cryoablation was undertaken under local or regional anaesthesia in 30 women (30/38; 79%).
- Significant decreases between initial median VAS score (7; IQR: 6, 8; range: 3–10) and median VAS score after treatment at three months (0; IQR: 0, 5; range: 0–8) ( $P < 0.001$ ), six months (0; IQR: 0, 1; range: 0–10) ( $P < 0.001$ ) and 12 months (0; IQR: 0, 2; range: 0–7) ( $P < 0.001$ ) were found.
- Percutaneous cryoablation resulted in effective pain relief in 31 out of 38 women (82%) at six months and 15 out of 18 women (83%) at 12 months.
- Contrast-enhanced MRI during six-month follow-up demonstrated a significant decrease in the volume of AWE nodules and the absence of AWE nodule enhancement after treatment by comparison with baseline MRI ( $P < 0.001$ ). No major complications were reported.

Bachour et al. [76] concluded that:

- Percutaneous cryoablation is an efficacious, minimally invasive intervention for the treatment of AWE nodules that conveys minimal or no morbidity.

## Conclusions

- Endometriosis of the kidney and urinary tract organs is an uncommon affliction which manifests with non-specific symptoms and signs that simulate the manifestations of more common afflictions of the kidney and urinary tract organs.
- Diagnosis of endometriosis of the kidney and urinary tract organs requires a high index of suspicion and pathology examination of specimens of the lesions.
- Even though most often endometriosis of the kidney and urinary tract organs had tended to be treated with analgesia to control pain as well as medicaments including hormonal treatment, definite treatment in a number of scenarios had required complete surgical excision of the lesion; nevertheless, pursuant to the development of minimal invasive surgery, alternative procedures could be used in the first instance to treat endometriosis of the kidney and urinary tract organs which include: cryotherapy of the lesion, radiofrequency ablation of the lesion, irreversible electroporation of the lesion, thermotherapy of the lesion, as well as selective angiography and super-selective embolization of the branch of artery supplying the lesion, pursuant to confirmation of the biopsy based upon pathology examination of the lesion.
- In the scenario of obstructed ureter and hydronephrosis, the initial management to improve or maintain renal function may entail the undertaking of per-cutaneous nephrostomy or cystoscopy, retrograde ureteropyelogram, ureteroscopy and insertion of double J ureteric stent to obviate the ureteric obstruction to enable good drainage of urine.
- Even though some individuals who are afflicted by endometriosis may manifest with a number of symptoms including infertility, endometriosis may not be the actual cause of infertility.

- It is important for all clinicians to appreciate the fact that female factor infertility may account for 40% of cases, male factor infertility may account for 40% of cases and 20% of cases may be attributed to a combination of male and female infertility factors. In view of this if a lady with endometriosis manifests with infertility, both the lady and her spouse should be fully investigated to ascertain the cause of the infertility in order to provide excellent management of each case.

## Conflict Of Interest – Nil

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