THE ROLE OF MAGNETIC RESONANCE IMAGING IN THE EVALUATION OF GYNECOLOGICAL DISORDERS.

DISSSERTATION SUBMITTED IN PART FULFILMENT FOR THE DEGREE OF MASTER OF MEDICINE IN DIAGNOSTIC IMAGING AND RADIATION MEDICINE, UNIVERSITY OF NAIROBI

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1.0 ACKNOWLEDGEMENT

First and foremost I wish to express my sincere gratitude to my supervisors Dr. A. Odhiambo, Dr. N. Waithaka and Dr. G. Mwango for their tireless guidance throughout this study.

To my fellow residents, lecturers and other members of staff, at the Department of Diagnostic imaging and Radiation Medicine for their encouragement and constructive criticism.

I also extend my gratitude to the MRI radiographers and support staff at Plaza Imaging Solutions who assisted me in data collection and the Kenyatta National Hospital.

Special thanks go to my husband, Dr. B. M. Osumba, for great support and also his contribution to my literature research.

2.0 DEDICATION

This work is dedicated to my twin daughters Apiyo and Adongo. They gave me strength to keep going.

To my husband Martin for the much needed love, support and encouragement.

To my parents who gave their best to give me a chance to have the best education.

3.0 DECLARATION

I, Dr. CHRISTINE AMO MAMAI declare that the work contained herein is my original idea and has not been presented for a degree at any other university to the best of my knowledge.

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4.0 TABLE OF CONTENTS

CONTENT

1.0 ACKNOWLEDGEMENT.	īi
2.0 DEDICATION	iii
3.0_DECLARATION	iv
4.0 TABLE OF CONTENTS	v
5.0 ABBREVIATIONS	vi
6.0_TERMINOLOGY	viii
7.0 ABSTRACT	<u>ix</u>
8.0 INTRODUCTION	1
9.0 LITERATURE REVIEW	
10.0 JUSTIFICATION	
11.0 MAIN OBJECTIVE	
11.1 SPECIFIC OBJECTIVES	
12.0 METHODOLOGY	
12.1 study area	
12.2 study population	
12.3 study design	
12.4 MRI pelvic scanning technique	
12.5 Inclusion/Exclusion criteria	
12.6 sample size	29
13.0 Data management	
14.0 Ethical consideration	32
15.0 Results	33
16.0 Representative images	
17.0 Discussion	
18.0 Conclusion	53

29.0 Recommendations	54
20.0 APPENDIX A: QUESTIONNAIRE	55
21.0 REFERENCES	58

FIGURES

Figure15.1: Study centers	
Figure 15.2: Age distribution of study patients (n=62)	
Figure 15.3: MRI as primary or secondary imaging modality (n=62)	
Figure 15.4: Clinical Indication (n=62)	
Figure 15.5: MIRI diagnosis – conclusive vs inconclusive (n=62)	

TABLES

Table 1: Presenting complaints	36
Table 2: MRI scan findings	
Table 3: Conclusive MRI diagnosis	40
Table 4: Patient age vs conclusive MRI diagnosis	
Table 5: Clinical Indication vs conclusive/inconclusive MRI diagnosis	
Table 6: Clinical Indication vs final MRI diagnosis	43

5.0 ABBREVIATIONS

- CNS Central Nervous System
- CT Computed Tomography Imaging.
- **DUB** Dysfunctional uterine bleeding
- FLAIR Fluid Attenuated Inversion Recovery
- GIT Gastrointestinal tract
- HPV Human Papilloma Virus
- i.e. That is
- IV Intra venous
- KNH Kenyatta National Hospital

Lt Left

MMED Masters Degree in Medicine

- MRA Magnetic Resonance Angiography
- MRI Magnetic Resonance Imaging
- PD Proton Density
- PIS Plaza Imaging Solutions, Nairobi.
- Rt Right
- SE Spin Echo
- SI Signal Intensity
- STIR Short Tau Inversion Recovery
- T Tesla
- TAS Trans abdominal Ultrasound
- TE Echo time
- TR Repetition Time
- TVS Transvaginal sonography.
- T1-WI T1 weighted images, with a short TR and a short TE
- T2-WI T2 weighted images with a long TR and a long TE
- UoN University of Nairobi
- US Ultrasound Scanning
- Vs Versus

6.0 TERMINOLOGY

SIGNAL INTENSITY – The radiofrequency radiation received from a structure in the body under interrogation. The signal may be bright, dark or intermediate.

T1 – is the longitudinal relaxation time; it represents time taken by the system of nuclei to return to thermal equilibrium after a radiofrequency pulse.

T1WI – heavily T1 weighted image; body tissue contrast is based mainly on short Repetition Time (TR) and a short Time to Echo (TE).

T2 – is the transverse relaxation time; it is the characteristic decay time of the free induction decay and is due to irreversible dephasing of the initially coherent precision of nuclei.

T2WI – Heavily T2 weighted image; body tissue contrast based mainly on a long TR and a long TE. This sequence shows zonal anatomy as well as pathology of pelvic viscera.

Proton Density (PD) images are obtained by minimizing effects of T1 and T2 thus resulting in long TR and a short TE

7.0 ABSTRACT

Background

Pelvic disease is a major cause of morbidity and mortality worldwide.²Studies have shown that MRI is invaluable in evaluating the female gynecological pelvis where Computed Tomography (CT) and Ultrasound (US) have been found to be inconclusive.³

Methodology

This was a prospective descriptive study at the Kenyatta National Hospital and the Plaza Imaging Solutions during the period November 2008 to April 2009. Sixty two (62) female patients referred for gynecological pelvic MRI were studied.

Objective

The objective of this study was to determine the pattern of pelvic disease seen in the gynecological patients using 1.5 Tesla MRI units at two MRI centers in Nairobi. The study also established the age, presenting complaints and indications of patients who were referred for MRI examination.

Results

Sixty two female patients with a mean age of 44.8 years and an age- range of 15years to 80years were included. 46 of the patients were referred for MRI as a secondary imaging modality after inconclusive US (54.0%) and inconclusive CT (19.0%) examinations. Assessment of carcinoma of the cervix was the commonest clinical indication (30.6%) followed by pelvic mass (24.2%). Pelvic mass was the most common presenting complaint at 39.9%. MRI diagnosis was conclusive in 90.3% cases with the commonest diagnosis being carcinoma of the cervix (28.6%).

Conclusion

MRI was a useful imaging modality in the evaluation of gynecological disorders. Its main application was in evaluating gynecological malignancy. It was also useful in the further evaluation of lesions in inconclusive ultrasound and Computed tomography examinations.

8.0 INTRODUCTION

Gynecological disorders have a wide spectrum including infections, benign and malignant lesions. The most frequently encountered conditions are benign but they contribute to a woman's quality of life and fertility.^{1,2} Magnetic Resonance Imaging has its main role in gynecologic oncology and in the evaluation of pelvic congenital anomalies³.

Magnetic resonance imaging (MRI) is a non invasive method of mapping the internal structures of the body.⁴ It employs radio frequency radiation in the presence of carefully controlled magnetic fields to produce high quality cross sectional images of the body in any plane.⁴ MRI does not employ ionizing radiation and its multiplanar & multisequential capabilities enable us to study the structure of interest in multiple views. Compared to CT and Ultrasound, MRI has excellent tissue contrast resolution which is even improved with higher field magnets (for example 3Tesla).The ability to use fast imaging (breath-hold & breath independent) helps reduce patient motion and gut peristaltic motional blur.

In the female pelvis, MRI provides the most comprehensive assessment of the pelvic organs of any imaging modality. Its applications are found in further evaluation of the pelvis where US or CT has been found to be inconclusive. MRI is invaluable in the staging of gynecological malignancies and it is now widely accepted as the optimal tool for the evaluation of the main prognostic factors and selection of therapeutic strategy⁵.

The role of MRI in gynecologic oncology has evolved during the past two decades. There is now a substantial body of evidence that MRI is useful in evaluating malignant conditions of the pelvis.^{1,6} MRI has been shown to be superior to CT in staging of endometrial and cervical carcinoma. In addition, there is evidence that MRI may aid in differentiating radiation fibrosis from recurrent tumor. The accuracy of MRI assessment of lymph nodes is similar to that of CT; both rely on size criteria to detect the presence of metastases⁶.

In Kenya, Cervical carcinoma is considered to be the commonest gynecological malignancy⁷, although its true incidence is unknown. It however has a prevalence rate of 1.2-3.8% in non-pregnant women worldwide.⁸ It is also the third most common gynecologic malignancy worldwide. Endometrial carcinoma is the fourth most common female cancer and the most common malignancy of the female reproductive tract worlwide⁹. In 2007, 39,080 new cases and 7,400 deaths were expected in the United States⁹. The incidence is rising because of increased life expectancy and obesity.

Uterine fibroids are the commonest tumors of the uterus and the female pelvis and are present in greater than 20% of women older than 30years worldwide.^{10,11} Among the Caucasians, fibroids are found in 20-25% of females of the reproductive age, but among blacks they are found more frequently at 35%. Wanjala¹², in 1975 & 1984 showed that fibroids constitute 1.6% of acute gynecological admissions and are the reason for 66.7% of hysterectomies at the Kenyatta National Hospital (KNH).

A descriptive prospective study was carried out at two MRI centers in Nairobi for a period of six months with an aim of determining MRI findings of the gynecologic pelvis. Similar 1.5Tesla Intera Phillips machines were used.

9.0 LITERATURE REVIEW

In 2007, a study was carried out by Evis et al¹ to review the role of MRI in the imaging of malignant neoplasms of the uterine corpus and cervix; and to describe its role in staging, treatment planning, and follow-up. MRI was shown to be significantly superior to sonography and CT in the evaluation of both tumor extensions into the cervix and myometrial invasion. The overall staging accuracy of MRI was reported to be between 85% and 93%. The routine use of dynamic IV contrast enhancement was shown to significantly improve the accuracy of the assessment of depth of myometrial invasion (accuracy of 55–77% for T2-weighted images versus 85–91% for dynamic contrast-enhanced images). They concluded that whereas MRI was not officially incorporated in the International Federation of Gynecology and Obstetrics (FIGO) staging system, it was already widely accepted as the most reliable imaging technique for the diagnosis, staging, treatment planning, and follow-up of both endometrial and cervical cancer. However MRI protocols needed to be optimized to obtain the best results and avoid pitfalls.¹

The recommendations for diagnostic evaluation of cervical tumor staging derive from the Tumor size, Nodes and Metastasis (TNM) and FIGO clinical staging systems. In single-institution studies, MRI has been shown to be better than either CT or physical examination in depicting parametrial invasion¹³. The staging accuracy of MRI ranged from 75% to 96%. A prospective multi-center study was conducted jointly by the American College of Radiology Imaging Network (ACRIN) and the Gynecologic Oncology Group (GOG) compared MRI, CT, and FIGO clinical staging in the pretreatment assessment of early invasive cervical cancer¹⁴. The study showed that MRI was equivalent to CT for overall preoperative staging. However, MRI performed significantly better than CT for preoperative tumor visualization and determination of parametrial invasion. Reviewer agreement was higher for MRI reviewers than for CT reviewers¹⁴.

Eun et al¹⁵ in 1999 sought to evaluate the role of MRI in staging of early endometrial carcinoma. They evaluated the usefulness of T2-weighted and gadolinium-enhanced T1-weighted magnetic resonance (MR) images correlated with patients' menopausal status in assessing the depth of myometrial invasion in stage 1 endometrial carcinoma. MR images of 46 patients with stage 1 endometrial carcinoma were retrospectively reviewed. Twenty-five patients were premenopausal, and 21 were postmenopausal. The staging accuracy without regard to menopausal status was 59% for T2-weighted images and 61% for gadolinium-enhanced T1-weighted images. However, when staging accuracy was evaluated separately in the premenopausal and postmenopausal patient groups, T2-weighted imaging had an accuracy of 80% in the premenopausal group and gadolinium-enhanced T1-weighted imaging had an accuracy of 81% in the postmenopausal group. Therefore, T2-weighted imaging was more accurate in premenopausal patients and gadolinium-enhanced T1-weighted imaging was more accurate in postmenopausal patients. The overall accuracy of staging with MR imaging improved to 80% when patients' menopausal status was considered. Therefore, menopausal status should be considered when T2-weighted and gadolinium-enhanced T1-weighted MR images are used to stage early endometrial carcinoma. These findings were attributed to the fact that in postmenopausal women, the junctional zone is usually poorly demonstrated on T2-weighted images, and there is no difference between the appearance of this zone on T2-weighted images and on gadolinium-enhanced T1-weighted images. In premenopausal women, however, the junctional zone is usually better demonstrated on T2-weighted images.^{1,15}

Magnetic resonance (MR) imaging has extended the usefulness of imaging in evaluation of pelvic disorders associated with female infertility. The causes of female infertility include ovulatory disorders (ie, pituitary adenoma and polycystic ovarian syndrome), disorders of the fallopian tubes (ie, hydrosalpinx and pelvic inflammatory disease), uterine disorders (ie, müllerian duct anomaly, adenomyosis, and leiomyoma), and pelvic endometriosis. MR imaging is used in a variety of clinical settings in diagnosis, treatment, and management such as congenital uterine anomalies, pituitary adenomas and pelvic endometriosis.³

In 2001, a radiologic-pathologic correlation study on endometriosis was done by Paula et al¹⁶. They found that radiologists were often involved in the diagnosis and work-up of this disease in one of two scenarios: They were asked to exclude endometriosis in a woman with pelvic pain or infertility or they were considering endometriosis in the differential diagnosis of an adnexal mass. Magnetic resonance imaging was found to improve diagnostic accuracy, with endometriotic cysts typically appearing with high signal intensity on T1weighted images and demonstrating "shading" on T2-weighted images. The ovaries were the most common sites affected, but endometriosis was also found to involve the gastrointestinal tract, urinary tract, chest, and soft tissues. The prevalence of endometriosis was difficult to determine accurately. Laparoscopy or surgery was required for the definitive diagnosis. Endometriosis has been reported in 4.1% of asymptomatic women undergoing laparoscopy for tubal ligation. However, in the same study, 20% of women undergoing laparoscopic investigation for infertility and 24% of women with pelvic pain had endometriosis. Overall prevalence, including both symptomatic and asymptomatic women, was estimated to be 5%-10%. They also found that gross pathologic findings of endometriosis depended on the duration of the disease and depth of penetration of the lesions. Endometriotic implants varied from punctate foci to small stellate patches (usually less than 2 cm). The amount of

pigment in the implant appeared to increase with the age of the lesion. They found that MR imaging had greater specificity for the diagnosis of endometriomas than other noninvasive imaging techniques. It afforded a larger field of view than US, and the effect of adhesions on surrounding anatomic structures was better depicted. Therefore, MR imaging can be a helpful adjunct for evaluation of adnexal masses.

Togashi et al¹⁷ in 1991 found that a "definitive" diagnosis of an endometrioma was made when a cyst was hyperintense on T1-weighted images and shading was observed on T2-weighted images. The diagnosis was also "definitive" when multiple hyperintense cysts were seen on T1-weighted images regardless of their signal intensity on T2-weighted images. In their study, MR imaging yielded an overall sensitivity, specificity, and accuracy of 90%, 98%, and 96%, respectively. Cyst appearance was variable because these cysts contained blood products of different ages and concentrations. Those lesions that were not hyperintense on T1-weighted images were difficult to distinguish from other adnexal masses.

Izumi et al¹⁸, in 2003, found MR imaging to be a useful modality as an adjunct for routine infertility work-ups. MRI was found to be valuable for detection of pituitary adenoma when patients are suspected of having a disorder of the hypothalamic-pituitary-ovarian axis. They also showed MR imaging being able to serve as an adjunct to diagnostic laparoscopy and hysterosalpingography for patients with hydrosalpinx, peritubal adhesions, or pelvic adhesions related to endometriosis.

Ewa et al¹⁹ in their review of overlooked and underdiagnosed gynecologic conditions causing pain, in 2005, found adenomyosis as an often-overlooked condition that was responsible for uterine enlargement and pelvic pain associated with dysmenorrhea and menorrhagia. The diagnosis of adenomyosis was, until then, rarely recognized before surgery. They also found that all patients with chronic pelvic pain were first examined with transvaginal US to identify whether fibroids, focal adenomyosis, or diffuse adenomyosis were present and to rule out other causes.

When transvaginal US findings are suggestive of adenomyosis, MR imaging is used as the definitive imaging modality for diagnosis. High-resolution transvaginal US and MR imaging can help establish the diagnosis of adenomyosis with a high degree of accuracy, since the imaging appearance closely correlates with the histopathologic characteristics of this entity. The first goal of transvaginal US and MR imaging is to establish the correct diagnosis for potential treatment. There are multiple conservative treatments possible for uterine fibroids, in contrast to debilitating extensive adenomyosis, for which hysterectomy is the only definitive treatment. The second goal is to determine the extent and depth of myometrial penetration for conservative treatment (endometrial ablation). The third goal is to monitor the evolution of the disease during conservative therapy.

A study by Robert²⁰ et al in 2002 to review the complementary role and contribution of magnetic resonance imaging (MRI) in gynecology diseases, found that MRI was becoming the complementary reference imaging tool for them. Its increasing indications were: gynecologic cancer, pelvis endometriosis, pelvis floor, indeterminate pelvis mass and fibroleiomyoma.

The role of MR imaging in patients with uterine leiomyoma includes the following : (a) differentiation between leiomyoma and adenomyosis; (b) anatomic localization of leiomyomas (subserosal, myometrial, submucosal, and cervical); (c) prediction of the outcome of treatments such as Uterine Artery Embolization (UAE) and Gonadotrophin Releasing Hormone (GnRH) analog therapy; and (d) monitoring for posttreatment changes and recurrences in patients treated with uterus-conserving methods.¹⁸ Leiomyomas typically demonstrate distinct low signal intensity relative to that of the myometrium on T2-weighted images and intermediate signal intensity on T1-weighted images. These characteristic signal intensities are attributed to extensive hyalinization, which occurs in more than 60% of uterine leiomyomas. However, leiomyomas can demonstrate various histopathologic patterns of degeneration, some of which alter the MR imaging appearance. Consistent with their benignity, leiomyomas have a "pushing" (instead of infiltrating) border and are rounded. However, several specific types of leiomyoma-intravenous leiomyomatosis, metastasizing leiomyoma, diffuse leiomyomatosis, and peritoneal disseminated leiomyomatosis - are exceptions to this rule.

In 1999, Hiroyuki et al²¹ studied the unusual appearances of Uterine Leiomyomas by looking at MR imaging findings and their histopathologic backgrounds at the Graduate school of Medicine, Kyoto University in Japan. They found that uterine leiomyomas demonstrated various types of degeneration, growth patterns, clinical courses, and complications. The MR imaging appearances of leiomyomas varied widely and presented a diagnostic problem. The differential diagnosis included a wide range of gynecologic and nongynecologic diseases. They therefore concluded that precise knowledge of the histopathologic background and clinical courses of leiomyoma allows a radiologist to distinguish leiomyoma with an unusual appearance from gynecologic malignancies.

In 2003, a study on racial differences in pelvic floor muscle thickness in asymptomatic nulliparous women using MRI- based 3D color thickness mapping was done in South Africa. This was done by Dowing et al²². They found that the

levator ani thickness was significantly greater in blacks bilaterally. However, the obturator thicknesses were similar in all races. They thought that these levator differences may influence pelvic floor dysfunction risk. However, the clinical significance of these findings is still under study.

From these studies, it has been seen that MRI as an imaging tool has a pertinent role in the diagnosis and further evaluation of gynecological disorders. This study has established the role that MRI plays, in our region, in the management of patients with gynecological lesions.

NORMAL FEMALE PELVIC ANATOMY ON MRI

The normal female pelvis contains the urinary bladder, uterus, fallopian tubes, ovaries, broad ligaments, muscles, rectum and blood vessels. The uterus lies between the urinary bladder anteriorly, and the rectum posteriorly with the ovaries and other adnexal structures on either side.

Pelvic anatomy is exquisitely demonstrated by MRI⁸. On T1- weighted sequences, the normal pelvic musculature and viscera demonstrate homogenous low to intermediate signal intensity. However it is the contrast resolution of T2-weighting that is the basis for the superb tissue characterization of MRI.⁷

The zonal anatomy of the uterus seen on T2WI shows 3 distinct zones, the high T2 signal endometrium, the low T2 signal junctional zone and the intermediate T2 signal myometrium.²³ The endometrium, composed of high signal glands, may measure up to 1.5cm in women of menstrual age & 5mm in postmenopausal women²⁴.On T1-WI there is poor distinction among the components of the endometrium and myometrium⁸.

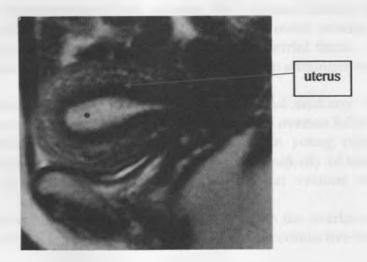


Figure 1- T2WI uterus in secretory phase

The cervix has a zonal anatomy that is well revealed on T2WI ²⁵. The central endocervical mucosa, secretions, and plicae palmatae have moderate to high Signal Intensity on T2WI; the middle layer has low SI and the outer layer low-to-intermediate T2-SI.

The vagina is a 7-9cm long, fibro muscular tube. Three normal zones of the vagina and paravaginal tissues are often depicted on T2WI²⁶. The vaginal muscles and collagen-rich submucosal layer appear as low T1, low T2 SI band.

Intraluminally, the vaginal mucosa and endoluminal secretions have low T1, high T2 SI.

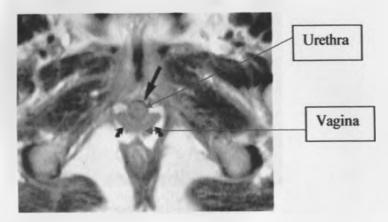


Figure 2- Axial T2WI shows H-shaped vagina outlined by high SI fat posterior to the urethra.

Following intravenous (IV) administration of paramagnetic gadolinium chelates, the zonal anatomy of the uterus is demonstrated on T1- weighted images. The endometrium and outer myometrium enhance to a greater extent than the junctional zone. Similarly, the inner cervical mucosa and outer smooth muscle enhance more than the fibromuscular stroma. The parametrial tissues, vaginal walls and submucosa also enhance after IV contrast medium administration.³

The ovaries in premenopausal women often reveal a zonal anatomy on T2WI with a lower SI ovarian cortex and a low-to-intermediate SI ovarian follicles^{27,28,29}

. Ovaries are classically ovoid and measure 3X2X2cm in young nulliparous women and 5X3X2cm in adult multiparous women. The majority of small cysts revealed within the ovary at MRI represent follicles at various stages of maturation.

In postmenopausal women there is decreased T2-SI within the ovarian medulla secondary to a paucity of follicles & decreased free vascular connective tissue.^{27,28}



Figure 3 - T2WI of the female pelvis.

The urinary bladder is optimally assessed on MRI by T2WI in which urine is of high SI while the bladder wall has low SI. The normal bladder wall measures 2mm when distended or less and 5mm or less when undistended ^{3,30}.

GYNECOLOGICAL DISORDERS

Classification

1. Congenital anomalies - include Mullerian duct anomalies and vaginal anomalies

2. Infective gynecological disorders- include pelvic inflammatory disorder, pelvic abscess

3. Neoplastic conditions

- Uterus: Benign neoplasms include uterine leiomyomas, adenomyosis, endometrial polyps, endometrial hyperplasia, Nabothian cysts
- malignant uterine neoplasms uterine sarcoma, endometrial carcinoma, gestational trophoblastic disease, cervical carcinoma.

- Ovaries - benign ovarian tumors and malignant ovarian tumors.

CONGENITAL ANOMALIES OF THE FEMALE GENITAL TRACT

These include Mullerian duct anomalies and vaginal anomalies.

Mullerian duct anomalies

Mullerian duct anomalies result from nondevelopmental or varying degrees of nonfusion or nonresorption of the Mullerian ducts. These anomalies occur in 1-15% of women and they are associated with menstrual disorders, infertility and obstetric complications. Renal anomalies may be present in up to 50% of these patients.³

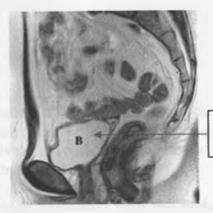
These anomalies include: - Mullerian agenesis or hypoplasia, Unicornuate uterus, Uterus didelphys, bicornuate uterus and septate uterus.

Class I-Hypoplasia or Agenesis. — Failure of normal development of the mullerian ducts causes uterine agenesis or hypoplasia. Patients present with primary amenorrhea in adolescence. In these cases, disorders of sexual differentiation should be excluded. It is necessary to document whether a functioning uterine corpus and cervix are present. For instance, a functioning uterine corpus and cervix are present. For instance, a functioning uterine corpus and cervix oprevent endometriosis.

Mayer-Rokitansky-Küster-Hauser syndrome is a combined anomaly that belongs to this entity. The typical form of this syndrome is characterized by congenital absence of the uterus and upper vagina. The ovaries and fallopian tubes are usually normal. The atypical form of the syndrome includes associated abnormalities of the ovaries and fallopian tubes and renal anomalies.



Figure 4



Urinary bladder

Figure 5

Figure 4 & 5 - Mayer-Rokitansky-Kuster-Hauser syndrome showing congenitally absent uterus and upper vagina.

Class II: Unicornuate. — Agenesis of a unilateral müllerian duct causes a single, socalled banana-shaped uterus with a single fallopian tube. On T2-weighted images, normal zonal anatomy is observed in a small uterus

Some patients have a rudimentary horn on the contralateral side. When the rudimentary horn is noncommunicating, endometrial tissue expelled retrogradely through the fallopian tube during menstruation results in an

increased frequency of endometriosis. This makes surgical resection of the horn necessary.

Spontaneous abortion and premature labor may occur in pregnancies with a unicornuate uterus, and the poorest fetal survival among all uterine anomalies has been reported.



Figure 6

Figure 7

Figure 6 & 7 - T2WI – Unicornuate uterus. Black arrow – unicornuate uterus White arrow-head – ovarian cyst

Class III: Didelphys. – Complete failure of fusion of the two mullerian ducts results in two complete uteri, each with its own cervix. T2-weighted images demonstrate two uterine horns or bodies with normal zonal anatomy. A longitudinal sagittal vaginal septum is usually, but not always, observed.

Among all uterine anomalies, uterus didelphys is associated with the highest possibility of successful pregnancy, except for arcuate uterus.

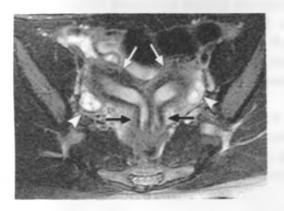


Figure 8 - T2WI – Uterine Didelphys Black arrows – two cervices

White arrows – fundal region of both uteri White Arrowheads - ovaries

Class IV: Bicomuate. — Partial fusion of two Müllerian ducts results in a bicornuate uterus with one cervix. The external uterine contour is concave or heart shaped, and the uterine horns are widely divergent. The MR imaging diagnostic criteria for bicornuate uterus are as follows: (a) divergent uterine horns with an intercornual distance exceeding 4 cm and (b) concavity of the fundal contour or an external fundal cleft more than 1 cm deep.

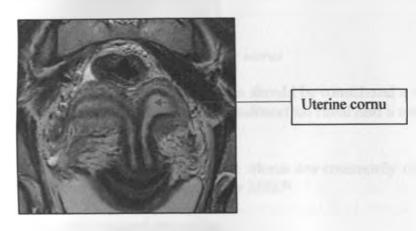


Figure 9 - T2WI- Bicornuate uterus

Class V: Septate. – Septate uterus results from failure of resorption of a septum after complete fusion of the mullerian ducts. The septum may be a combination of both fibrous tissue and muscle. A fibrous septum is demonstrated as low signal intensity on T2-weighted images, whereas a septum composed of abundant muscular tissue shows intermediate signal intensity.

The external uterine contour is normally convex, flat, or minimally indented by less than 1 cm, in contrast to that of a bicornuate uterus. T2-weighted images taken along a "true" coronal view of the uterine body and perpendicular to the long axis of the uterus provide exact images of the uterine contour and septum. This helps in differentiation of bicornuate from septate uterus.

Most patients evaluated for repeated abortions and found to have a uterine anomaly will have a septate uterus. Metroplasty is a surgical procedure used for treatment of this anomaly and may enhance fetal survival, with one report indicating that 95% of patients became pregnant, 73% carried to term, and 77% delivered a liveborn baby.

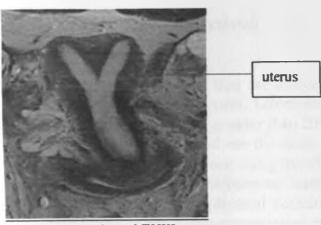


Figure 10 - MRI axial T2WI- septate uterus

Class VI: Arcuate. Arcuate uterus should be considered a normal variant, with a small indentation of the fundal endometrial canal and a normal external contour. It has no effect on fertility.

Developmental anomalies of the uterus are commonly detected by US but are more completely characterized by MRI.³¹

Congenital vaginal anomalies

Disorder of vertical fusion- the transverse vaginal septum prevents loss of menstrual blood and results in haematocolpos. Most patients present as teenagers with cyclic abdominal pain and a haematocolpos might be palpable within the pelvis. In these patients a careful pelvic examination and US are helpful for diagnosis. On MRI, T2W images show dilatation of the vagina with intraluminal fluid of intermediate or high signal intensity and the occasional presence of fluid/debris levels. The lower third of the vagina is replaced by low signal intensity fibrous tissue with loss of normal zonal anatomy.

Disorders of lateral fusion- These patients often present with the incidental finding of a vaginal septum that is usually asymptomatic. It may first be diagnosed during pregnancy and excision will be necessary to ensure a vaginal delivery.

ACQUIRED GYNECOLOGICAL DISORDERS.

BENIGN UTERINE CONDITIONS

UTERINE LEIOMYOMAS

These are benign neoplasms that are derived from the smooth muscle myoma cells of the uterine myometrium. Leiomyomas are the most common uterine neoplasms and are present in greater than 20% of women older than 30years ^{10,33}. They are usually multiple and are the most common cause of enlargement of a non-pregnant uterus. They are categorized by location as being intramural, subserosal or submucosal. Subserosal leiomyomas can mimic solid adnexal lesions on sonography and physical examination ^{27,34}, but MR can distinguish these two based on the direct communication of the fibroid with the uterus and the typical low SI on T2-WI ³⁴.

Hyaline and cystic degeneration is very common and calcification is often seen. Their malignant potential is very low (0.2%).

Ultrasound can detect most of these masses but their appearance is extremely variable, and degenerated pedunculated subserosal fibroids may simulate an ovarian carcinoma. Small fibroids in women of reproductive age are typically solid, arise from the uterus and have a whorled pattern. Malignant change within the fibroids is impossible to discriminate sonographically from benign counterparts¹⁰.

Leiomyomas having a paucity of intercellular matrix result in characteristic low SI on T2-WI ^{35,36}. They are well circumscribed with well-defined margins. Approximately one third of uterine fibroids are surrounded by a high SI rim on T2-WI that correlate with peritumoral lymphatics, veins, and oedema. MR has shown very high accuracy in detection and characterization of leiomyomas and the distinction between fibroids and adenomyosis ³⁷.

MRI can also characterize a submucosal-intracavitary leiomyoma as the cause of an endometrial mass.³⁸ MRI can document the size, number, location, and vascularity of uterine fibroids. MRI-Magnetic Resonance Angiography (MRA) provides data to determine mode of treatment which includes Uterine Artery Embolisation, and also follow-up. Post-uterine Artery Embolisation, MR has documented a decrease in volume of fibroids by 40% to 60% and decreased enhancement of fibroids, in keeping with successful necrosis ^{39,40}.

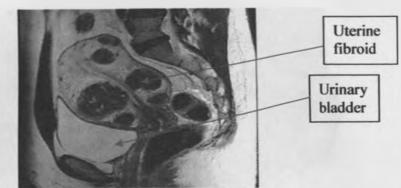


Figure 11 - Sagittal T2WI showing multiple leiomyomas

UTERINE ADENOMYOSIS

This is defined as the presence of endometrial tissue within the uterine myometrium. It is due to invasion of ectopic endometrium into myometrium with hyperplasia of adjacent smooth muscle and is usually either diffuse (67%) or focal (33%). It presents most frequently with dysmenorrhoea and Dysfynctional Uterine Bleeding (DUB). ^{3,41} It typically presents in multiparous women aged 40-50 years with dysmenorrhoea and DUB.

Transabdominal or Tranvaginal sonography is commonly used as the initial imaging modality. Adenomyosis may be missed on transabdominal ultrasound. At transvaginal sonography, typical features include poorly marginated hypoechoic and heterogenous areas within the myometrium, myometrial cysts, and globular or enlarged uterus with asymmetry.

MR can detect and characterize uterine adenomyosis by showing both the ectopic endometrial glands within the junctional zone and the surrounding smooth muscles. The short axis measurement of the junctional zone that is equal to or more than 12mm is diagnostic; 8mm or less adenomyosis is excluded with high specificity; between 8mm and 12mm is indeterminate^{35, 42}.

Hyper-intense 2- to 4mm foci on T2-WI within the thickened junctional zone represent embedded endometrial glands and add specificity to the MR diagnosis ⁴³. Adenomyosis compared to leiomyoma reveals poorly defined margins, is often oriented parallel to the endometrial stripe, and has minimal mass effect on the endometrial canal, whereas fibroids are well defined and do show mass effect ³⁵.

MR can more accurately diagnose adenomyosis than can transvaginal sonography⁴⁴, especially in women with coexistent leiomyomas⁴⁵. In some patients, the thickened junctional zone may mimic a thickened endometrium on transvaginal sonography.

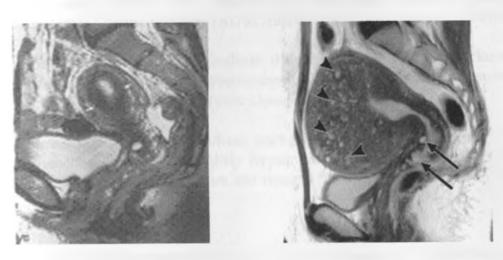


Figure 12

Figure 13

Figure 12 & 13 - SagittalT2WI showing uterine adenomyosis Black arrow heads- endometrial glands within the thickened myometrium Black arrows – Nabothian cysts

ENDOMETRIAL POLYPS

These are localized, pedunculated or broad-based growths of endometrial tissue that commonly cause bleeding. Benign endometrial polyps are common at all age groups, greatest in more than 50year olds but may be a cause of infertility in younger patients. They must be differentiated from submucous fibroids and malignant neoplasm.

On routine tranvaginal sonography, the polyps appear as a non-specific echogenic thickening of the endometrium. They appear as a filling defect on conventional Hysterosalphingogram. US- Hysterosalphingogram can delineate it but cannot differentiate broad based polyp from a submucous fibroid ³.

MRI shows a central fibrous core and intralesional cyst formation, but tissue sampling is needed to exclude endometrial carcinoma.

ENDOMETRIAL HYPERPLASIA

Endometrial hyperplasia is a proliferation of endometrial glands, which increase in size and assume an irregular shape. The hyperplasia is caused by unopposed stimulation of the endometrium by estrogen. Hormone replacement therapy with only estrogen is the most common cause of hyperplasia in post-menopausal women. In pre-menopausal women, causes include recurring anovulatory cycles, polycystic ovary disease, and obesity. Hyperplasia may be focal or diffuse, and is classified as cystic type (simple), adenomatous (complex) and atypical hyperplasia. Up to 25% of patients with endometrial hyperplasia with atypia will eventually present with endometrial carcinoma. Clinical presentation is Abnormal Uterine Bleeding (AUB), infertility and postmenopausal bleeding.

Ultrasonographic features include diffuse or focal smooth thickening of the endometrium, (>14mm in premenopausal women, >5mm in post-menopausal women with bleeding) and cystic changes are common.

On MRI, T2-WI- shows diffuse thickening of endometrial stripe with Signal Intensity iso-intense or slightly hypointense relative to normal endometrium. However these characteristics are nonspecific and are also seen in endometrial carcinoma³.

UTERINE INFECTIONS

Uterine infections most often occur in the puerperium. Endometritis might also be caused by septic abortion or post-operatively. Pyometra might occur in patients with cervical stenosis due to carcinoma of the cervix or following radiotherapy, or as a complication of endometritis. The distended uterus may be identified on US or cross-sectional imaging studies. The uniform thick-walled appearance of the distended uterus and failure to identify the uterus as a separate structure should differentiate the appearance from a pelvic abscess.

NABOTHIAN CYSTS

These are benign retention cysts that develop secondary to obstruction of the mucin-secreting endocervival glands by overgrowth by squamous epithelium. They are more common in multiparous women and women with prior cervicitis. When present, they are multiple and measure less than 2cm ⁴⁷. They are of no clinical significance.

On sonography, they appear as simple cysts and the internal fluid is anechoic except in rare instances when traumatic hemorrhage or infection results in internal debris.

On MR, nabothian cysts reveal variable SI on T1-WI that reflects the viscosity of the mucin cyst content. On T2-WI, most reveal high Signal Intensity. They do not enhance after contrast. ⁴⁸

MALIGNANT UTERINE CONDITIONS

ENDOMETRIAL CARCINOMA

This is the fourth most common cancer in women (with breast, lung, and colon cancer being the first three common) and the most common gynaecologic malignancy worldwide. Of the 10 most common cancers in women, endometrial carcinoma is the most curable⁴⁹. It affects mostly postmenopausal women with an age range of 55-65years⁵⁰. The most common symptom is postmenopausal bleeding.

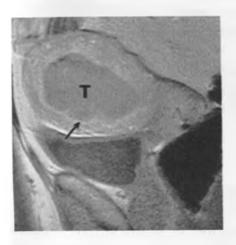
Transvaginal Sonography or endometrial biopsy should be performed as the initial procedure of choice in the evaluation of postmenopausal bleeding ⁵¹. US shows thickening of the endometrium that is often indistinguishable from hyperplasia and polyps. Signs that suggest cancer include inhomogenous echogenicity, irregular and poorly defined margins, and invasion of the myometrium.

MR is not recommended as a screening tool. It is used instead in staging a known cancer. It can distinguish between superficial and deep muscle invasive tumors by using a combination of T2-WI and dynamic Contrast Enhanced MR. MR has a higher staging accuracy than do sonography and CT. ^{52,53,54}

On T2-WI, endometrial carcinoma can have a variable appearance but typically appears as a heterogeneous endometrial mass that is hyperintense to adjacent myometrium and can have hypointense, isointense, and hyperintense components relative to normal endometrium. Hyperintense tissue that extends into more than half the width of the myometrium is the criterion for establishing muscle invasive tumor.

A staging MR may predict the presence or absence of malignant adenopathy based on the presence or absence of muscle invasion of the primary tumor. This can also direct the gynecologist and the patient on the best mode of treatment.

Secondary uterine and cervical cancers are uncommon and most result from direct extension from either bladder or colonic tumors, or extension of ovarian tumors via the fallopian tube.



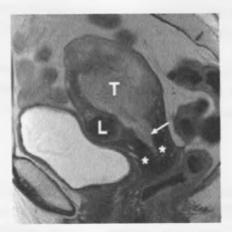


Figure 15

Figure 16

Figure 15 - TIW + gadolinium – endometrial carcinoma stage IB. T – thickened endometrium Figure 16 - T2WI- Stage IIA endometrial carcinoma. T- endometrial mass L – uterine fibroid

UTERINE SARCOMA.

Constitute only 3% of all uterine cancers, 97% are from endometrial glands. In decreasing frequency, the most common sarcomas are malignant mixed mullerian tumor (MMMT), leiomyosarcoma, and endometrial stromal sarcoma⁵⁵.

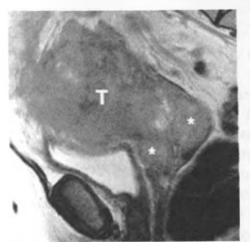


Figure 17 - T2WI- Malignant Mixed mullerian tumor

GESTATIONAL TROPHOBLASTIC DISEASE

Gestational trophoblastic neoplasms include the tumor spectrum of hydatidiform mole, invasive mole (choriocarcinoma destruens) and choriocarcinoma. They arise from fetal tissue within the maternal host and are composed of both syncitiotrophoblastic and cytotrophoblastic cells. The role of imaging in these diseases has been primarily to document metastatic disease at initial diagnosis or to evaluate persistent disease. As yet there are no specific imaging findings that allow differentiation of complete mole from invasive mole or choriocarcinoma.

On T2- weighted images, gestational trophoblastic disease is seen as a heterogenous, predominantly high signal intensity mass that obliterates normal uterine zone anatomy. On T1WI, it may be iso- or hyperintense to adjacent myometrium⁵⁶.

CERVICAL CANCER

The true incidence of cancer of the cervix in Kenya is unknown although it is the most common gynecological carcinoma, as seen by Ojwang SBO⁷ in 1985. Kimani²⁵ in his study of the pattern of female pelvic disease as shown on ultrasonography found cervical mass in 4.1% of the subjects.

Cervical cancer is the third most common gynaecologic malignancy in women in the United States of America (after endometrial and ovarian cancer). Screening for cervical cancer is done by annual Papanicolau (pap) smear beginning at age 18 or the onset of sexual activity, whichever comes first.⁵⁷

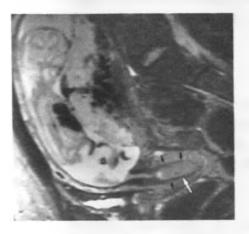
The Mean age of women with cervical cancer is 50years. Symptomatic women have bleeding or a vaginal discharge,⁵⁸ while asymptomatic women are diagnosed by Pap smear or by detection of an occult lesion on speculum exam. ⁵⁸ HPV types 16 & 18, tobacco, oral contraceptives use, history of herpes simplex infection, immunosuppressed host, and high sexual activity seem to be positively correlated to the disease. ³

Cancers of the cervix are primarily diagnosed clinically. Early cervical cancer is difficult to detect on ultrasound whether TransAbdominal or Transvaginal Sonography. More advanced cancer can be visualized on Tranvaginal Sonography (that is beyond Stage IIB). During Ultrasonography, the cervix is seen as an irregular hypoechoic mass that may mimic a cervical fibroid. If the tumor obstructs the endocervical canal, hydrometra, haematometra, or pyometra may result. With transrectal Ultrasound, the uterine cervix, parametrium, vagina, pelvic sidewall, rectum and posterior bladder can be visualized. For stage II, III and IV, ultrasound detects or shows the extent of the disease. It is also helpful in the evaluation of metastasis to organs such as the liver. It may be used for staging but CT and MRI are preferable.

CT typically shows enlarged cervix, but distinguishing tumor from normal tissue, the cervix and parametrium may be problematic.

MRI has superior soft tissue contrast between tumor and normal tissue, & the ability to define tumor in orthogonal planes. On T2-WI, characteristic feature of cervical cancer is an intermediate SI mass. Tumor Signal Intensity is usually greater than normal low Signal Intensity found in the fibro cervical stroma. On T1-WI, tumors are usually isointense with normal cervix and may not be visible. Intravenous contrast media highlights tumor heterogeneity and aids in differentiation of viable tumor from debris and necrosis ⁵⁹. This also helps evaluate bladder and rectal involvement.

Cross sectional imaging is recommended in evaluating cervical cancer patient with clinical stage IB disease when the primary lesion is greater than 2cm ⁶⁰. MRI is the best single imaging investigation for this purpose, since it's better than either CT or physical examination in demonstrating parametrial invasion and as good as CT in detecting nodal metastases ⁶¹.





Cervical mass

Figure 18 Figure 19 Figure 18 - Sagittal T2WI showing breech pregnancy and cervical cancer (arrows).

Figure 19 - Sagittal T2WI showing cervical carcinoma

OVARIES AND ADNEXAE

Kimani²⁵, in 2000 showed adnexal disease to be common in female patients who underwent pelvic ultrasonography at the KNH. Tubo-ovarian mass was the commonest adnexal lesion, found in 35.9%. Other studies have shown that among pelvic masses, benign adnexal masses are the commonest accounting for 34%.⁶²

Pathology of Benign ovarian tumors

Physiological cysts include follicular cysts and luteal cysts.

Benign Germ cell tumors are common in less than 30year old females and only 2-3% are malignant. They include dermoid cysts and mature teratoma.

Benign Epithelial tumors constitute majority of ovarian neoplasms, both benign and malignant. They include serous, mucinous& endometriod cystadenoma and Brenner's tumor.

Benign sex cord stromal tumors include granulosa cell tumors, theca cell tumors, fibroma and sertoli-leydig cell tumor.

MRI can diagnose dermoid cysts with confidence as fat or sebum within the cyst parallels the Signal Intensity of fat on all pulse sequences. Simple cysts appearance is diagnostic low Signal Intensity on T1-WI, High Signal Intensity on T2-WI and no enhancement post Intravenous contrast media.

The real strength of MRI is its ability to characterize adnexal lesions, especially in the case of US indeterminate masses.

Malignant ovarian conditions

Ovarian neoplasms account for more cancer related deaths than all other primary pelvic cancers. In general, ovarian cancer is a disease of post-menopausal women and occasionally pre-pubescent girls. Although the cancer is usually curable in its early stages, two-thirds of all patients have tumor spread beyond the pelvis when the diagnosis is made.

Imaging features suggestive of malignancy include ascites, large sizes, complexity, the presence of solid components and an irregular wall.

Major histopathological categories of ovarian cancers include:- Epithelial e.g. serous and mucinous cystadenocarcinoma, Germ cell type e.g. dysgerminoma, sex cord and stromal like fibromas and metastatic cancers to the ovary e.g. breast, colon, stomach, endometrial and lymphoma. Epithelial tumors account for 85% of ovarian cancers and they arise from the surface epithelium and the mesothelium of the outer ovarian cortex. These tumors are classified as benign (cystadenoma), borderline malignant (formerly called tumors of low malignant potential), and malignant (cystadenocarcinoma).

Differentiating benign from potentially malignant ovarian lesion is a primary goal of US. Unfortunately, no single gray-scale or Doppler US finding reliably provides this differentiation.³¹

CT is the most commonly performed study for the preoperative evaluation of a suspected ovarian cancer. MRI is not a cost-effective screening modality. However a study done by Kurtz AB et al ⁵⁴, showed that compared with CT and US, MR was superior in characterization of malignant ovarian lesions.

It is estimated that up to 35–45% of women with advanced ovarian cancer can be optimally debulked without pre-procedural chemotherapy. Either CT or MRI can define the tumor burden within the abdomen and pelvis to determine which women might benefit from pre-operative chemotherapy.

Endometriosis

This is perhaps the most prevalent cause of chronic pelvic pain, occurring up to 65% of women with pelvic pain. ^{63, 64}

Endometrial tissue is present outside the uterus in the pouch of Douglas, ovaries, covering the peritoneum of bowel and bladder. Endometriosis usually affects women of the reproductive age, and it clinically presents with dysmenorrhoea, dyspareunia, abdominal pain, Dysfunctional Uterine Bleeding & infertility.

On MRI, endometriomas are hyperintense on T1-WI & heterogeneously hyperintense on T2-WI.⁶⁴ The use of fat suppression increases conspicuity of endometriosis.⁶⁵ MRI has been advocated as a non-invasive technique to monitor treatment response and some investigators have suggested using MRI to help select appropriate candidates for hormone therapy (e.g. Gonadotrophin releasing Hormone).⁶⁵

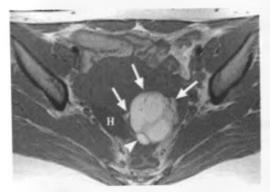


Figure 20 Figure 20 -Axial TIWI- ovarian endometrioma White arrow – left ovarian endometrioma

OTHER IMAGING MODALITIES OF GYNECOLOGICAL DISORDERS

ULTRASONOGRAPHY

Ultrasonography is an imaging modality that utilizes high frequency sound waves to interrogate the human body.

Common indications of female ultrasonography include abnormal uterine bleeding, Pelvic mass, suspected fibroids, history of recurrent abortions, Infertility, Follicular monitoring for patients on fertility drugs, suspected uterine abnormalities.

Some of its advantages include: - Relatively inexpensive, widely available, does not involve ionizing radiation, mobile systems are available and can be taken to the bedside and operating theatres.

Its limitations include: it is operator dependent and image quality varies with patient body habitus. Ultrasound is also low in spatial resolution hence not as useful as either CT or MRI in the staging of pelvic malignancies ⁽³⁾.

COMPUTED TOMOGRAPHY.

This is an imaging modality that utilizes X-rays to create an image. X-rays being ionizing radiation is not favorable in women in the reproductive age group who desire future fertility.

CT made a recent entry in imaging of the female pelvis but is applied mainly for the evaluation and staging of malignancy. In the developed world, CT is seldom used except where MRI is unavailable and Ultrasound is inconclusive. In our local set up, CT is continually being used in the staging of most pelvic malignancies including cervical cancer and ovarian tumors.

A pitfall in the use of CT in evaluating female pelvic disease is the low soft tissue contrast resolution. It is however good in showing extension of disease to the bony pelvic wall.

HYSTEROSALPINGOGRAPHY

This is an imaging test whereby radio-opaque contrast media is instilled into the uterus and fallopian tubes. It is mainly used to evaluate infertility.

10.0 JUSTIFICATION

Gynecological disorders are a major cause of morbidity and mortality in our society and the world at large. The common presenting complaints are pelvic mass, chronic pelvic pain and menorrhagia. These symptoms can be debilitating to a working patient as much time is lost when the patient is away from work. Most of the affected are in the reproductive age group and still desire fertility. Proper diagnosis and management of these conditions therefore go a long way in preserving or restoring their fertility and quality of life.

MRI is a non-invasive superior imaging tool of the gynecologic pelvis.² It does not involve ionizing radiation,⁴ hence is safe for patients who desire future fertility. Various studies have shown that MRI is invaluable in the evaluating malignant conditions of the pelvis; ^{1,6} and it is now widely accepted as optimal for evaluation of the main prognostic factors and selection of therapeutic strategy⁵. Its applications are found in further evaluation of the pelvis where ultrasonography or Computed Tomography has been found to be inconclusive.²⁰

No prior study to evaluate the role of MRI on gynecologic disorders had been done in Kenya. Most studies available are from the developed world. There was therefore need to find out the role of MRI as a diagnostic and follow-up tool in management of female pelvic disease in our set up.

The aim of the researcher was to determine the indications for gynecologic MRI examination, determine the pattern and frequency of gynecological disorders in patients undergoing pelvic MRI examination and most importantly to determine in which conditions MRI makes a significant impact.

This study was also a baseline and audit platform for future studies on the role of specialized imaging techniques in gynecology.

RESEARCH QUESTION

What is the role of MRI in assessing the gynecologic pelvis in Kenya?

11.0 MAIN OBJECTIVE: - To show the pattern of lesions detected by MRI examination of the gynecologic pelvis as seen at the Kenyatta National Hospital and Plaza Imaging Solutions.

11.1 SPECIFIC OBJECTIVES:

- 1. To determine the indications for gynecologic MRI examination in our set up.
- 2. To determine the pattern and frequency of gynecological disorders in patients undergoing pelvic MRI examination.
- 3. To find out the age distribution of female pelvic pathology at MRI.
- 4. To determine the conditions in which MRI provides additional information in patients who have had a prior US or CT examination.

12.0 METHODOLOGY

12.1 Study area

This study was carried out at two MRI centers in Nairobi, Kenya, namely Kenyatta National Hospital and Plaza Imaging Solutions.

12.2 Study population

All female patients, of all age groups, with gynecological complaints, referred to the two MRI centers for Pelvic MRI study.

12.3 Study Design

This was a descriptive prospective study that was undertaken from November 2008 to April 2009. Patients' clinical summary (age, serial number, Indication, and other radiological investigations done) was obtained from the request form and filled into the data collection form (Appendix A). The MRI findings were reviewed by the researcher and a consultant Radiologist and recorded in the data collection forms.

MATERIALS

Same model of MRI machine, 1.5 Tesla Phillips Intera was used in the two centers.

12.4 MRI PELVIS SCANNING

Patient preparation

Complete patient history was taken including the menstrual cycle, prior pelvic surgery and any device or foreign body in the pelvis including an Intra-Uterine Contraceptive Device or tampon. Any contraindication to MRI exam including pacemaker, aneurysm clip or inner ear implant was ruled out. Patients fasted for 4-6 hours so as to limit bowel motion or alternatively they were given an antiperistaltic (hyoscine butyl bromide) just before going into the MRI examination room. They were also asked to empty bowel and the urinary bladder immediately before the examination.

Receiver Coils

Surface body coils were used in the two centers. These are transmit-receive coils hence providing a homogenous magnetic field with a good signal-to-noise ratio.

Standard MRI Imaging Protocol

Contiguous 5mm thick slices were done in the following sequences and pulses:

- T1W sequence in axial, coronal and sagittal planes
- T2W sequence in axial, coronal and sagittal planes
- T2W SPAIR in axial, coronal and sagittal planes.

The researcher reviewed the images in collaboration with the consultant radiologist, and directed on the need to give Intravenous contrast media. The intravenous contrast agent used was Gadolinium (DTPA), which is non-toxic and well tolerated even by patients with renal insufficiency. It was given in a bolus fashion at a dose of 0.1mmol/kg using a pump injector.

Gadolinium was given in the following situations:-

- 1. Poorly defined or suspicious lesions on pre-contrast images.
- 2. Patients sent for assessment of tumor recurrence or residual tumor post surgery, chemotherapy or radiotherapy.
- 3. Histological proven tumor for assessing tumor extent

No oral contrast was given to the patients.

12.5 Inclusion /Exclusion Criteria

All female patients referred for pelvic MRI examination for gynecological disorders in the two MRI centers.

Patients excluded from the study included:-

- 1. Patients who had contraindications for MRI evaluation such as pacemaker, brain aneurysm clips, inner ear implants or were in first trimester pregnancy.
- 2. Patients who opted for another examination like computed tomography due to claustrophobia.
- 3. Female patients undergoing pelvic MRI examination for nongynecological reasons.

12.6 Sample size calculation.

As MRI has its main role in gynecologic oncology, cervical carcinoma with a prevalence rate of 1.2-3.8% in non-pregnant women worldwide⁸ is also the third most common gynecologic malignancy. It is considered to be the most common gynecological malignancy in Kenya.⁷ Kimani²⁵ in his study of the pattern of female pelvic disease as shown on ultrasonography found the prevalence of cervical mass was 4.1%. The p value therefore was 3.8%.⁸

Sample size was determined by the following formula by Fisher et al (1998) 66

n = <u>z² p (1-p)</u> d² Where n = desired sample size z = standard normal distribution (1.96) p = known prevalence rate of cancer of the cervix at 3.8%. ⁸ d = the level of significance desired (0.05)

Substituting these values in the above formula:-

 $n = \frac{(1.96)^2 \times 0.038(1 - 0.038)}{(0.05)^2}$

n=56

The proposed sample size was 56 subjects. The actual study population was sixty two patients (n=62). A preliminary survey indicated twelve (12) patients undergo gynecological MRI study in the two study centers each month. The study period was therefore taken to be six months.

Sampling method

Consecutive sampling method was used. All patients undergoing female pelvic MRI examination in the two MRI centers during the six month period (November 2008-April 2009) were included in this study. No distinction in sample distribution was made.

Limitations of the study

- 1. The main limitation of this study was sampling bias in that the population was of only those patients who had been referred for pelvic MRI study by the clinicians. Also majority of the patients were oncology cases. Therefore, the sample did not include patients with the more common gynecological diseases.
- 2. Due to the relative high cost of MRI study, not all patients who required pelvic MRI were referred. This study sample was most likely from a high socioeconomic status.
- 3. No local studies had been done in Kenya or Africa on gynecological MRI to compare the findings with.
- 4. **Radiological diagnosis was the final diagnosis**. No histological diagnosis was availed to correlate with.

Standardization of Radiological Results

Similar MRI machine models and imaging protocols were used in the two study centers (1.5Tesla Phillips Intera unit). This ensured reproducibility of the images taken.

The researcher reviewed the request forms and MRI images of all the patients included in the study and formed a radiological opinion. Each case was then discussed by the researcher and the consultant radiologist for a consensus opinion. The consensus opinion was the radiological diagnosis.

13.0 Data Management

After data collection, all the raw data was entered into a computer. Data analysis was done using software program for social science research (SPSS). Results have been presented in the form of frequency distributions and descriptive statistics. Representative images of some of the conditions seen have also been presented.

14.0 ETHICAL CONSIDERATIONS

- 1. Approval was sought from KNH Ethics and Research committee.
- 2. The patient's name did not appear anywhere in the data collection form in order to maintain confidentiality.
- 3. No examination was done on a patient apart from the one requested by the primary physician. For this reason there was no need for signed consent.
- 4. Information obtained from the study was treated with total confidentiality and results used for academic and clinical improvement purposes only. The study did not interfere with the management of the patients in any way.
- 5. The results of this study will be availed to the heads of health management teams in the two MRI centers, to colleagues and students in the medical college fraternity.

A total of 62 patients were reviewed during the study period. The results are presented below.



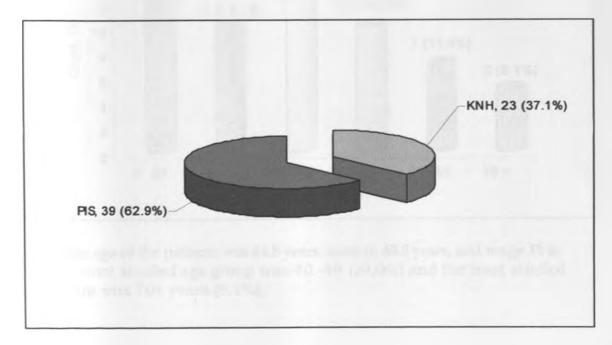


Figure 15.1: shows the distribution of the study sample between the 2 study centers. 39 (62.9%) cases were collected at Plaza Imaging Solution while 23 (37.1%) from KNH.

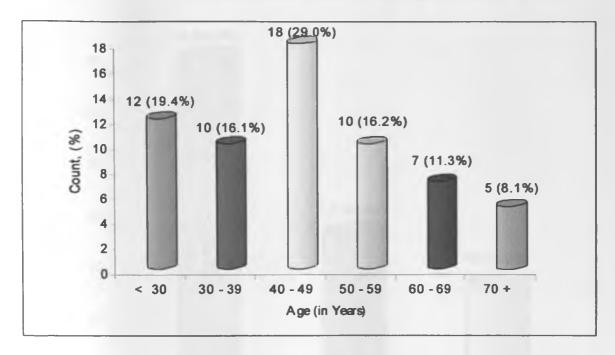


Figure 15.2: Age distribution of the study patients (n = 62)

The mean age of the patients was 44.8 years, median 43.5 years, and range 15 to 80. The most studied age group was 40 -49 (29.0%) and the least studied age group was 70+ years (8.1%).

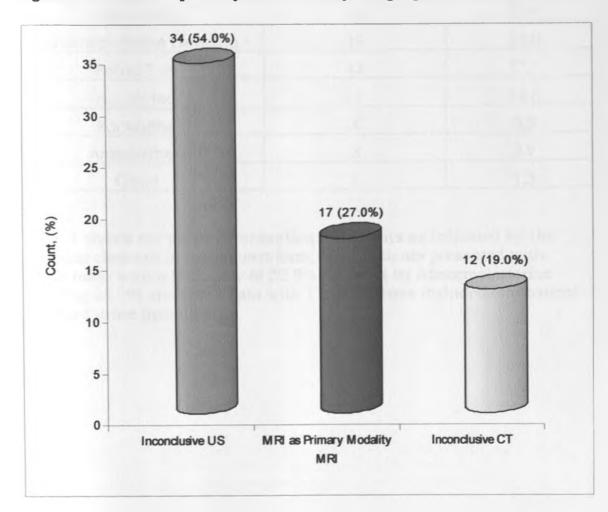


Figure 15.3: MRI as primary or secondary imaging modality (n=62)

Most of the patients (73.0%), as indicated in the request forms and demonstrated in table 2 were referred for MRI examination as a secondary imaging modality. Of these, 54.0% were after inconclusive pelvic ultrasonography while 19.0% cases had inconclusive Computed Tomography study. 27.0% patients were referred for MRI as a primary imaging modality.

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Complaint	Frequency	Percent
Pelvic Mass	25	32.9
Abnormal Uterine bleeding	19	25.0
Pelvic Pain	13	17.1
Not stated	11	14.5
Backache	4	5.3
Amenorrhea	3	3.9
Other	1	1.3

Table 1: Presenting Complaints (as per the request forms)

Table 1 shows the patients presenting complaints as indicated by the referring clinician in the request form. Most patients presented with pelvic mass with a frequency of 32.9%, followed by Abnormal uterine bleeding 25.0% and pelvic pain with 17.1%. Others included one patient who had urine incontinence.



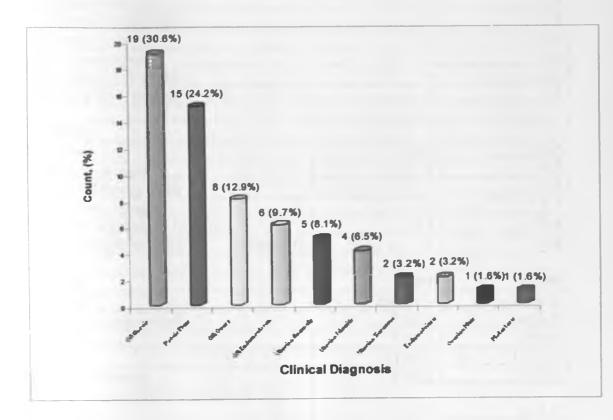


Figure shows the clinical indication for referring the patients for pelvic MRI examination. This was as indicated in the request form. The commonest clinical indication was carcinoma of the cervix with a frequency of 30.6%, pelvic mass 24.2%, carcinoma of the ovary 12.9%, carcinoma of the endometrium 9.7%, Uterine anomaly at 8.1% and uterine fibroids 6.5%. The least common indication was metastasis and ovarian mass at 1.6% each.

In overall, gynecological malignancies, whether suspected or histologically proven accounted for 56.4%. These included cancer of the cervix, cancer of the ovary, endometrial cancer and uterine sarcoma.

Uterus	Frequency	Percent
Normal	24	38.1
Fibroids	7	11.1
Adenomyosis	3	4.8
Endomentrial Mass	4	6.3
Absent (TAH)	15	23.8
Myometrial Mass	3	4.8
Congenital anomaly	4	6.3
Other (PID 1, Hydrometra 2)	3	4.8
Cervix		
Normal	37	59.7
Nabothian cyst	3	4.8
Non-infiltrating mass	1	1.6
Infiltrating mass	6	9.7
Absent (Aplasia 2, TAH 10)	12	19.4
Other (Radiotherapy 2, Stenosis 1)	3	4.8
Ovary	Right	Lef
Normal	38 (61.3)	40 (64.5
Benign ovarian cyst	4 (6.5)	4 (6.5
Ovarian ca	1 (1.6)	3 (4.8
Absent	10 (16.1)	11 (17.7
Endometrioma	2 (4.8)	0 (0.0)
Others (atrophic 2, ovotestis 2, enlarged 7)	7 (11.3)	4 (6.5)
Vagina		
Normal	56	90.3
Mass	5	8.1
Absent	1	1.6
Urinary Bladder		
Normal	56	90.3
Wall thickening	5	8.1
Infiltrating Mass	1	1.6
Pelvic Floor & Wall		
Normal	46	74.2
Lymphadenopathy	2	3.2
Fluid in cul-de-sac	8	12.9
Infiltrated parametrium	2	3.2
Others (1Dermoid cyst, 1pelvic sarcoma,		
2pelvic masses)	4	6.5

Table 2: MRI Scan Findings (n=62)

One patient may have had multiple MRI findings in different pelvic organs.

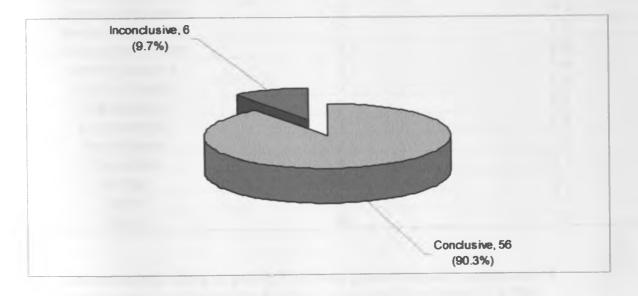


Figure 15.5: MRI Diagnosis- conclusive vs inconclusive (n=62)

MRI findings were conclusive in 90.3% of the cases. No further imaging modalities were required. In 9.7% the results were inconclusive and correlation with other imaging modalities (ultrasonography or micturating cystourethrogram) was suggested.

	Frequency	Percent
Cancer of the Cervix	16	28.6
Cancer of the Ovary	8	14.3
Simple Ovarian cyst	1	1.8
Endometrial Cancer	5	8.9
Uterine Sarcoma	3	5.4
Uterine Fibroids	5	8.9
Adenomyosis	2	3.6
Endometriosis	1	1.8
Pelvic Mass	1	1.8
Congenital	4	7.1
Normal	6	10.7
Other	4	7.1
Total	56	100

Table 3: Conclusive MRI diagnosis (n=56)

The commonest finding at pelvic MRI was gynecological malignancies combined (cancer of the cervix (28.6%), cancer of the ovary (14.3%), endometrial carcinoma (8.9%) and uterine sarcoma (5.4%). Others include dermoid cyst (1) and Pelvic Inflammatory Disease (2) and pelvic sarcoma in a patient who had been treated for cancer of the cervix.

	Age Distribution						
MRI Diagnosis	< 30	30 - 39	40 - 49	50 - 59	60 - 69	70 +	Total
CA Cervix	1	1	9	3	1	1	16
CA Ovary	1	0	1	2	1	2	7
CA Ovary + Simple Ovarian							
Cyst	0	0	0	0	1	0	1
Simple Ovarian Cyst	1	1	0	0	0	0	2
Endometrial Carcinoma	0	0	1	0	3	0	4
Uterine Sarcoma	0	0	1	3	0	0	4
Uterine Fibroids	1	1	0	1	1	0	4
Uterine Fibroid + Adenomyosis	1	0	0	0	0	0	1
Adenomyosis	0	0	2	0	0	0	2
Endometriosis	1	0	0	0	0	0	1
Congenital Anomaly	4	0	0	0	0	0	4
Normal	0	4	1	0	0	1	6
Others	1	1	1	0	0	Ţ	4
Total	11	8	16	9	7	5	56

Table 4: Patient Age Vs MRI conclusive diagnosis

The commonest age group with pelvic pathology was 40-49 years and the least was 70+ years. Of note is that at 40 - 49 age groups, the commonest lesion was cancer of the cervix.

Some patients had more than one pathologies. The combinations included uterine fibroid + adenomyosis; cancer of the ovary and simple ovarian cysts.

	Final MRI	Diagnosis	Total
Clinical Indication	Conclusive	Inconclusive	
CA cervix	17	2	19
Ca Ovary	6	1	7
Ca Endometrium	5	0	5
Uterine Sarcoma	2	0	2
Uterine Fibroid	3	1	4
Congenital Anomaly	5	0	5
Pelvic Mass	13	2	15
Endometriosis	2	0	2
Metastasis	1	0	1
Ovarian Mass	1	0	1
CA ovary + Endometriosis	1	0	1
Total	56	6	62

Table 5: Clinical indication vs Conclusive / inconclusive MRIdiagnosis

MRI radiological diagnosis was highly sensitive. The findings were conclusive in 90.3% cases. Of the 9.7% inconclusive cases, 2patients were suspected clinically to have cancer of the cervix, 1 cancer of the ovary, 1 uterine fibroid and 2 had indeterminate pelvic masses.

Table 6: Clinical Indication vs Final MRI findings

		Final MRI Findings													
Clinical Indication	CA Cervix	CA Ovary	CA Ovary	+ Simple Ovarian	Simple Ovarian	Endo. Carcinoma	Uterine Sarcoma	A. 10	Fibroid + Adenomyo	Adenomyo	Endometrio	Congenital Anomaly	Normal	Others	
CA cervix	15	s c		C) 0	0	C			0	C	0 0	1		1
CA Ovary	0	6 10		C	0	0	C	0	0	0	0	0 0	0	,	0
CA Endometrium	0	0 0		С) 0	4	C	1	0	0	0	0)	0
Uterine Sarcoma	C	0 0		C) 0	0	2	0	0	0	0	00	C	1	0
Uterine Fibroid	C	C		C	0 0	0	C	2	0	1	0	0	C	>	0
Congenital Anomaly	0	0 0		C	0, 0	0	C	0	1	0	0	4	C		0
Pelvic Mass	1	1		1	2	0	1	1	0	1	1	0	2	/	2
Endometriosis	0	C C		C	0 0	0	C	0	0	0	0	0	1		1
Metastasis	0) (C	0 0	0	C	0	0	0	0	00	1		0
Ovarian Mass	0	0 10		C	0 0	0	0	0	0	0	0	0	1	_	0
CA ovary + Endometriosis	0			C) C	0	1	0	0	0	0	0	0		0
Total	16	> 7		1	2	4	4	4	1	2	1	4	6	2	4

Table 6: correlates the clinical indication as per the request form with the conclusive MRI diagnosis.

17.0 REPRESENTATIVE IMAGES

Figure 17.1:-Multiple uterine fibroids in a 34 year old.

T2W sagittal image showing multiple intramural and one fundal subserosal fibroid. A nabothian cyst is seen as a focus of hyperintensity in the posterior cervical wall.
Coronal T2W image showing multiple uterine fibroids.
T1W image + intravenous gadolinium showing homogenous enhancement of intramural fibroids.

Figure 17.2:- Huge intramural uterine fibroid in a 26 year old female.

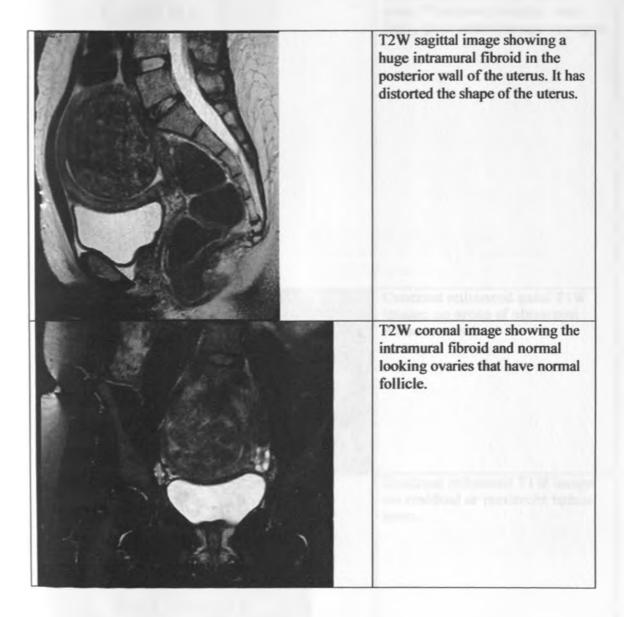


Figure 17.3:- A 51 year old patient with carcinoma of the cervix post Total abdominal hysterectomy and radiotherapy. The uterus is absent and there is thickening of the urinary bladder wall.

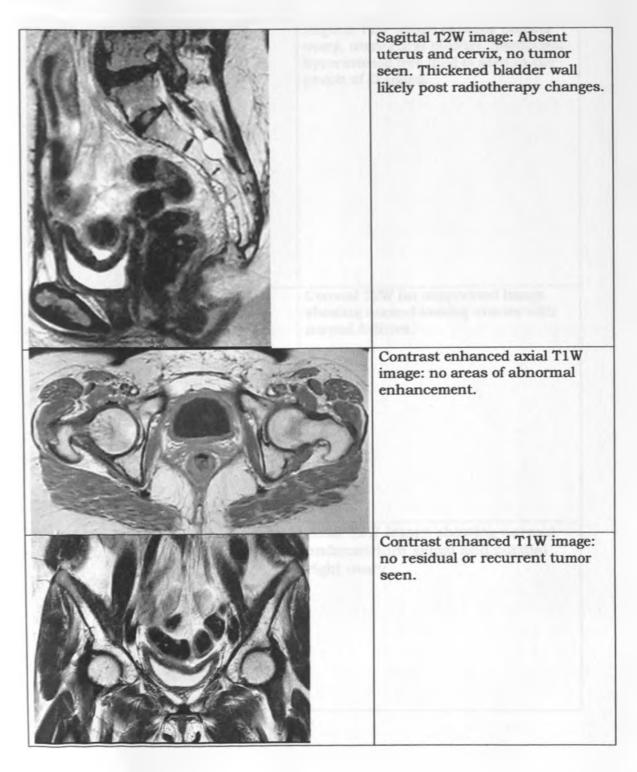
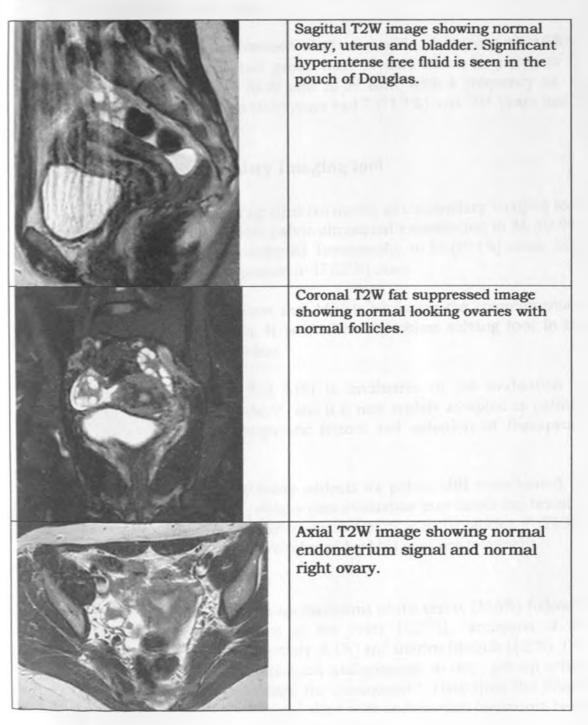


Figure 17.4:- A 29 year old female with features of pelvic inflammatory disease



17.0 DISCUSSION

Age Distribution

The age range of the patients examined was 15 years to 80 years with a mean age of 44.8 years and median 43.5 years.

The commonest age group was between 40-49 years with a frequency of 29.0% of the sample. The second commonest group was <30years with a frequency of 12 (19.4%). The third group was 30-39 and 50-59 each with a frequency of 10 (16.2%). The age group between 60-69years had 7 (11.3%) and 70+ years had 5 (8.1%).

MRI as a primary or secondary imaging tool

MRI was requested by the referring clinician mostly as a secondary imaging tool. It was requested after inconclusive pelvic ultrasound examination in 34 (53.9%) cases and due to inconclusive computed Tomography in 12 (19.1%) cases. MRI was a first imaging modality requested in 17 (27%) cases.

Other authors ⁽²⁰⁾ have also shown that MRI is becoming the complementary reference imaging tool for them. It is used as a problem solving tool in the evaluation of gynecological disorders.

Various studies have shown that MRI is invaluable in the evaluation of malignant conditions of the pelvis; ^{1,6} and it is now widely accepted as optimal for evaluation of the main prognostic factors and selection of therapeutic strategy⁵.

In this study the reasons for referring patients for pelvic MRI were varied. 24 (38.1) patients were referred for pelvic organs evaluation post tumor treatment to check for treatment response, tumor recurrence or new malignancies. 7 (11.3%) cases with pelvic malignancies were referred for MRI scan pre-treatment.

Clinical Indication

The commonest clinical indication was carcinoma of the cervix (30.6%) followed by pelvic mass (24.2%), carcinoma of the ovary (12.9%), carcinoma of the endometrium (9.7%), congenital anomaly (8.1%) and uterine fibroids (6.5%). This conforms to the pattern of gynecological malignancies in our set up where carcinoma of the cervix is considered the commonest.⁷ Data from the West ⁸ shows carcinoma of the cervix to be the third with endometrial carcinoma being the commonest followed by carcinoma of the ovary. Most of the cases of malignancies (38.7%) were referred for evaluation for residual tumor, tumor recurrence or treatment response as opposed to further evaluation before initial treatment (11.3%). This implies that MRI is yet to be incorporated as a work up tool for patients with gynecological malignancies before treatment in our set up. Other studies ¹ have shown that whereas MRI was not officially incorporated in the International Federation of Gynecology and Obstetrics (FIGO) staging system, it was already widely accepted as the most reliable imaging technique for the diagnosis, staging, treatment planning, and follow-up of both endometrial and cervical cancer.

Discussion on MRI findings in the study population

A total of 62 patients were scanned. Out of these 56(90.3%) had a conclusive MRI findings and diagnosis while 6 (9.7%) cases had inconclusive MRI findings. Out of the conclusive MRI findings 6 (10.7%) were found to be normal scans while 50 (89.3%) had pathology. Therefore MRI had a sensitivity of 90.3% in this study.

The Uterus

24 (38.4) uteri were found to be normal with their zonal anatomy well outlined in T2 weighted images. 15 (23.5%) were absent post hysterectomy.

Uterine fibroids

Leiomyomas are the most common uterine neoplasms and are present in greater than 20% of women older than 30years ^{10,33}. They are usually multiple and are the most common cause of enlargement of a non-pregnant uterus. Ultrasound can detect most of these masses and only indeterminate cases may require MRI evaluation.

Wanjala¹², in 1975 & 1984 showed that fibroids constitute 1.6% of acute gynecological admissions and are the reason for 66.7% of hysterectomies at the Kenyatta National Hospital (KNH). This study had 5 (8.9%) cases of uterine fibroid. This small frequency may be explained by the high sensitivity of Ultrasound examination. Majority of these patients aged 60-69years, while 50 - 59years and 70+ ages had no fibroids.

Adenomyosis

This condition presents as hyper-intense 2- to 4mm foci on T2-WI within the thickened junctional zone representing embedded endometrial glands adding specificity to the MR diagnosis.⁴³ These features were seen in 3 (4.8%) cases. Two (2) patients were in the 40-49 years age group and 1 was <30 years old.

Endometrial carcinoma

MR is not recommended as a screening tool in this condition. It is used instead in staging a known cancer. It can distinguish between superficial and deep muscle invasive tumors by using a combination of T2-WI and dynamic Contrast Enhanced MR. ^{52,53,54}

Endometrial carcinoma affects mostly postmenopausal women with an age range of 55-65years⁵⁰. The most common symptom is postmenopausal bleeding. This study had 4 (6.3%) cases with endometrial carcinoma. These were patients who had inconclusive pelvic ultrasound examination. Most of these patients (3) were between 60 – 69years while one (1) case was in the 30-39year age group. The main presenting complaint was abnormal uterine bleeding (AUB).

Uterine sarcoma

These constitute only 3% of all uterine cancers, 97% are from endometrial glands. In decreasing frequency, the most common sarcomas are malignant mixed mullerian tumor (MMMT), leiomyosarcoma, and endometrial stromal sarcoma⁵⁵.

Three 3 (5.4%) cases in this study had uterine sarcoma seen as heterogenous myometrial mass with moderate and heterogenous contrast enhancement. Other series ⁶⁷ showed 2 (5.3%) out of 60 cases of mixed mullerian sarcoma. The prevalence in these two studies is similar.

The three (3) patients were between 50-59 years old.

Congenital genital anomaly

There were 4 (6.3%) cases of congenital anomaly. All were <30 years old and presented with infertility. Two of them had bicornuate uterus that was contributing to the infertility while two patients had Mullerian agenesis. Patients with Mullerian agenesis had absent uterus, absent cervix and a single enlarged ovary (ovotestis).

Other uterine lesions included 1 case of Pelvic Inflammatory disease (PID) and 2 cases of hydrometra one of which was secondary to cervical stenosis.

Cervical Carcinoma

Cancers of the cervix are primarily diagnosed clinically. Early cervical cancer is difficult to detect on imaging. Cross sectional imaging is recommended in evaluating cervical cancer patient with clinical stage IB disease when the primary lesion is greater than 2cm. ⁶⁰

Majority of the patients referred with a diagnosis of cervical cancer were referred for disease analysis post- treatment. Only a small percentage was referred for tumor evaluation pre-treatment.

Cervical carcinoma was the commonest gynecological malignancy reported in this study. It was diagnosed in 16 (28.6%) cases. This figure compared to 19 patients who had a clinical diagnosis of carcinoma of the cervix, 6 (9.7%) cases showed infiltrating mass on MRI, 1 (1.6%) non- infiltrating mass, 10 (19.4%) cases had absent cervix post Total Abdominal Hysterectomy and no mass, while 2 cases showed post radiotherapy changes.

Other studies in the Western world have shown 20% of 60 patients with primary genital tract tumor to have carcinoma of the cervix but endometrial carcinoma was the commonest diagnosis.⁶⁷

The age distribution of carcinoma of the cervix in this study showed 40-49years leading with 9 cases, followed by 50-59years. Patients <30years had one case. This concurs well with the known peak age of cancer of the cervix.³

The Ovaries and adnexae

38(61.3%) right ovaries and 40 (64.5%) left ovaries were found to be normal with normal looking stroma and follicles. 4 (6.5%) right and 4 (6.5%) left ovaries had benign simple ovarian cysts.

Cancer of the ovary was seen in 8 cases (14.3%). 4 cases (7.1%) had ovaries removed due to carcinoma of the ovary. Imaging features suggestive of malignancy included large sizes, complexity, the presence of solid components and an irregular wall. Six (6) out of the 8 cases of cancer of the ovary were seen in patients above 50 years which is a perimenopausal age group. Literature shows cancer of the ovary to be a disease of postmenopausal women.³

The two (2) cases suspected to have endometriosis ended up being normal (1) and pelvic inflammatory disese (1). Ovarian endometrioma was however found in 1 (1.8%) patient <30years old who had been clinically diagnosed with a pelvic mass. Demaerel et al⁶⁷ showed one (1) case of endometrioma. This study concurs with other series that the diagnosis of endometrioma is a rare feature.

Kimani²⁵, in 2000 showed adnexal disease to be common in female patients who underwent pelvic ultrasonography at the KNH. Tubo-ovarian mass was the commonest adnexal lesion, found in 35.9%. Other studies have shown that among pelvic masses, benign adnexal masses are the commonest accounting for 34%.⁶² Benign adnexal masses were few in this study and included simple ovarian cysts (8), dermoid cyst (1) and endometrioma (1). This emphasizes that MRI does not play a major role in benign pelvic disease in our set up.

Pelvic floor and wall

Normal pelvic floor and wall was seen in 46 (74.2%) patients. Regional lymphadenopathy was seen in 2 (3.2%) patients with carcinoma of the ovary indicating metastatic disease.

Free fluid in the cul-de-sac was found in 8 (12.9%) of which 2 patients had cancer of the cervix, 2 cancer of the ovary, 1 cancer of the endometrium, 1 patient with cervical stenosis and 2 patients with pelvic inflammatory disease.

The parametrial tissues were infiltrated by tumor in 2 (3.2%) cases. These were patients with cancer of the ovary.

18.0 CONCLUSION

- 1. MRI in our setup is used as a secondary imaging modality. It is being used as a problem solving tool where ultrasound and has been found to be inconclusive. This may also be explained by the relatively high cost of MRI hence it is not available to most population.
- 2. MRI of the female pelvis is mainly used in evaluation of gynecological malignancies in our set up. Majority of the patients are sent for assessment post-treatment.
- 3. Carcinoma of the cervix is the commonest gynecological malignancy in our country affecting mostly 40-49years age group. MRI application is mainly found in patient evaluation post- treatment.

19.0 RECOMMENDATIONS

- 1. Where it is affordable, MRI needs to be incorporated into evaluation of the gynecological disorders especially where ultrasonography is inconclusive. This will increase the diagnostic confidence enabling proper planning for patient management.
- 2. Radiohistopathological correlation study needs to be done to assess the specificity of MRI in assessing gynecological diseases. Picking on one organ and reviewing MRI features of pathology will also go a long way to establish disease presentation in our set up.

20.0 APPENDIX A: - SAMPLE QUESTIONNAIRE

А.	PATIENT'S BIODATA
	Serial no
	MRI center
	Age in years
	□ Pre-menopausal □ Post-menopausal
В.	MRI AS PRIMARY OR SECONDARY IMAGING MODALITY 1. MRI as first imaging modality 2. MRI as a secondary imaging modality a. In inconclusive US b. In inconclusive CT
C.	 PRE- OR POST- TREATMENT 1. Pre-treatment Tumor staging 2. Assess tumor post treatment 3. Others (specify)
D.	CLINICAL INDICATION 1. CA cervix 2. CA ovary 3. CA endometrium 4. Uterine sarcoma 5. Uterine fibroids 6. Congenital anomaly 7. Pelvic mass 8. Others – specify a. Adenomyosis b. Endometriosis c. Metastasis d. PID e. Ovarian mass
E.	 Presenting complaints (indicated on the request form) 1 .Pelvic pain 2. Pelvic Mass 3. Abnormal Uterine Bleeding 4. Amenorrhea 5. Not stated 6. Backache 7. Others

F. MRI scan findings

UTERUS

- 0. Normal
- 1. Fibroids
- 2. Adenomyosis
- 3. Endometrial mass
- 4. Absent
- 5. Myometrial mass
- 6. Others

RT OVARY

- 1. Normal
- 2. Ovarian mass
 - 2.1. Benign Cyst
 - 2.2. Ovarian ca
- 2. Absent
- 3. Endometrioma
- 4. Others

VAGINA

- 0. Normal
- 1. Mass
- 2. Absent

PELVIC FLOOR & WALL

- 0. Normal
- 1. Lymphadenopathy
- 2. Infiltrated parametrium
- 3. Fluid in cul-de-sac
- 4. Others (specify).....

CERVIX

- 0. Normal
- 1. Nabothian cyst
- 2. Non-infiltrating mass
- 3. Infiltrating mass
- 4. Absent a) Aplasia b) TAH
- 4. Others (specify).....

LT OVARY

- 0. Normal
- 1. Ovarian mass
 - 1.1. Benign cyst
 - 1.2. ovarian ca
- 2. Absent
- 3. Endometrioma
- 3. Others

URINARY BLADDER

- 0. Normal
- 1. Cystitis
- 2. Infiltrating mass

G. Other prior imaging studies (if available) and findings.

- 0. Ultrasound
- 1. Computed Tomography
- 2. Others (specify).....

H. MRI diagnosis

- 1. Conclusive
- 2. Not conclusive

I. CONCLUSIVE MRI DIAGNOSIS

1. Ca cervix with no tumor

- 2. Ca cervix with tumor
- 3. Ca cervix- Absent cervix no tumor
- 4. ca ovary with tumor

5. Ca ovary no recurrence

6. Simple ovarian cyst

7. Endometrial Ca

- 8. Uterine sarcoma
- 9. Uterine fibroids
- 10. Adenomyosis
- 11. Endometriosis
- 12. Pelvic mass non-specified
- 13. Congenital anomaly
- 14. Normal
- 15. Others

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