Fixed learning module

Benign tumours of uterus

Dr.Rasika Herath
Department of Obstetrics and Gynaecology
Faculty of Medicine, University of Kelaniya

Contents

1. Abbreviations

AUB-Abnormal Uterine Bleeding
ART-Assisted Reproductive Technique
COCP-Combined Oral Contraceptives
D&C-Dilatation and Curettage
FET-Frozen Embryo Transfer
FIGO-International Federation of Gynaecology and Obstetrics
HMB-Heavy menstrual bleeding
HRT-Hormone Replacement Therapy
IMB-Intermenstrual bleeding
LNG-IUS-Levonorgestrel intrauterine system
NSAIDS-Non Steroidal Anti-Inflammatory Drugs
PAECs-Progesterone receptor modulator-associated endometrial changes
PMB-Post Menopausal bleeding
PR-Progesterone receptor
SIS-Saline Infusion Sonography
SPRMS-Selective Progesterone Receptor Modulators
TRS-Tissue Removal Systems
TSH-Thyroid Stimulating Hormone
TVS-Transvaginal Ultrasonography
UAE-Uterine Artery Embolization
UPA-Ulipristal acetate
USS-Ultrasonography

2. Objectives

- The student should be able to describe the incidence, risk factors, pathology, clinical presentation, complications and diagnosis of endometrial polyps and fibroids.

- The student should be able to have an understanding of the advantages and disadvantages of the different treatment options available for polyps and fibroids.

- Student should be able to describe pre-op preparation (including consenting) of women for myomectomy

- Student should be able to describe post-op management of women who has undergone a myomectomy

- Student should have basic understanding of the procedure of open/laparoscopic/Hysteroscopic myomectomy which is needed for consenting for a woman

- Student should have a reasonable understanding of different request forms/consent forms used in patients undergoing surgery

Types of benign tumours

Benign gynaecological tumours contribute to significant proportion of women presenting to gynaecologist with menstrua problems. In this FLM we will be discussing two common problems; endometrial polyp, uterine fibroids.

3. Endometrial polyp

Endometrial polyps are discrete endometrial outgrowths that can occur anywhere within the uterine cavity. They contain a variable amount of glands, stroma and blood vessels, and individual proportion change their visual appearance at ultrasonography(USS)and hysteroscopy.

They may be soft and cystic or firm and fibrous, pedunculated or sessile, single or multiple and vary in sizes.

3.1 Prevalence

Endometrial polys are mostly asymptomatic and some are never diagnosed. If untreated most of the polys will remain, though some small polys may regress spontaneously. The prevalence varies depending on the population studied.

- Among general adult female population without Abnormal Uterine Bleeding(AUB): 10-15%
- Among women with AUB: 10–20%
- Infertile women without AUB: 6-11%
- Asymptomatic post-menopausal women undergoing Transvaginal ultrasonography(TVS): 13%

The majority of uterine polyps are benign. It is estimated that 0.2-23.8% of polyps to have endometrial hyperplasia without atypia, 1-3% have atypical hyperplasia. The prevalence of endometrial cancer in a polyp is about 1% among symptomatic women.

3.2 Aetiology and risk factors

The mechanism of formation of uterine polyp remains unclear, though thought to be multifactorial. They would start as focal areas of stromal and glandular overgrowth within the endometrium. The effect of hormones on polyp formation is unclear and they do not appear to be sensitive to the normal cellular mechanisms that regulate the endometrium. Therefore, polyps remain relatively insensitive to cyclical hormonal changes, leading them to persist despite regular menstruation.

The known risk factors include Obesity, late menopause, use of tamoxifen and estrogen only hormone replacement therapy (HRT).

3.3 Clinical presentations

Abnormal uterine bleeding is the most common symptom of endometrial polyps. They may present as heavy menstrual bleeding (HMB), intermenstrual bleeding (IMB), post-menopausal bleeding (PMB) or dysmenorrhoea. If the polyp is large and protruding out of the cervix the woman may develop post coital bleeding also. The mechanism by which endometrial polyps induce these different patterns of AUB remains uncertain, though possibly linked to altered responses to oestrogen and progesterone compared with the background endometrium, inflammatory changes and disturbed angiogenesis seen within the polyp.

Infertility is one of the impotent presentation among younger females with polyps probably hampering endometrial receptivity and thus implantation failure. Polyps are considered amongst other intrauterine factors, such as congenital uterine anomalies and acquired structural cavitary defects like leiomyomas and synechiae that might contribute to infertility and recurrent pregnancy loss. How polyps contribute to subfertility and pregnancy loss is still uncertain, but mechanical interference with sperm transport, embryo implantation, through intrauterine inflammation or increased production of inhibitory factors has been postulated.

3.4 Diagnosis

Endometrial polyps will not give rise to any significant examination finding, unless they are very large and protruding out of the cervix. In such cases the polyp may be visible during the speculum examination.

A diagnosis of a polyp can be arrived by three approaches

1. Ultrasonography
2. Hysteroscopy
3. Biopsy

3.4.1 Ultrasonography

Ultrasonography offers easy and simple way of assessing endometrial cavity with minimal discomfort to the patient. The availability, and ability to give information about other uterine pathologies such as fibroids and adenomyosis, make USS the first line investigation in assessing women with suspected endometrial polyp. Transvaginal ultrasonography approach is preferred in this regard and is more accurate when performed in the proliferative phase of the menstrual cycle, when the endometrium is thin, makes it easier to see the polyp.

Ultrasonographic finding of non-specific endometrial thickening or a focal mass identified as an echogenic lesion, which disturbs the midline endometrial echo but does not disrupt the interface between the myometrium and endometrium, is identified as an endometrial polyp (Figure 1).

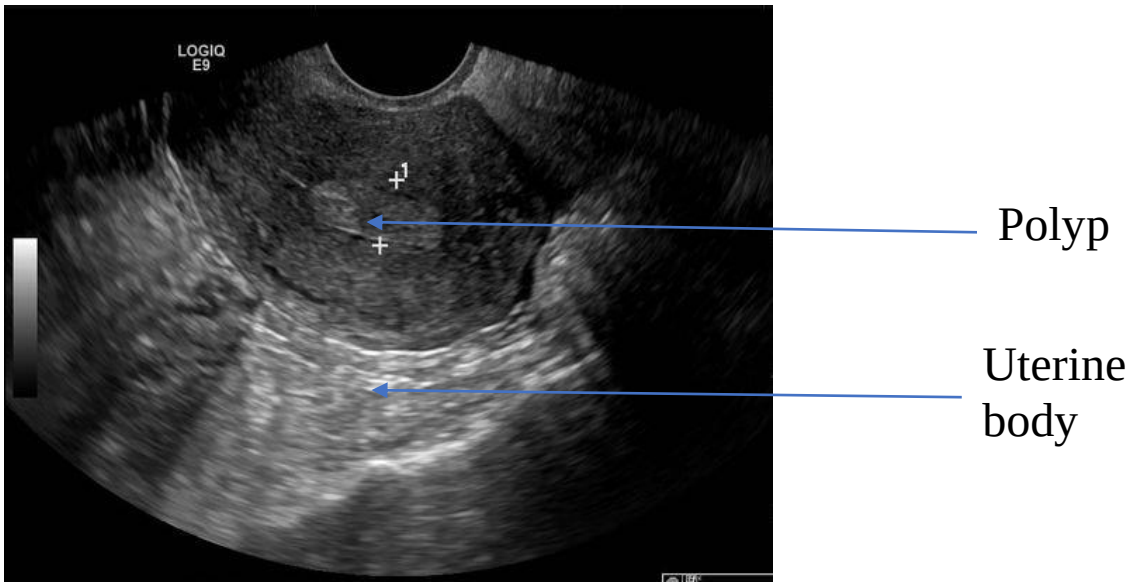


Figure 1- Transvaginal ultrasonography showing an endometrial polyp

The addition of saline, which is non-echogenic, in to the uterine cavity while evaluating with Ultrasonography is called saline infusion sonography (SIS). These techniques improve diagnostic accuracy compared with TVS alone. During SIS the fluid allows better contrast within the endometrial cavity clearly delineating the stalk of the polyp and improving detection of smaller polyps, which may have been missed during TVS (Figure 2). More recently colour Doppler and 3D ultrasonography has been used more frequently to evaluate endometrial polyps.

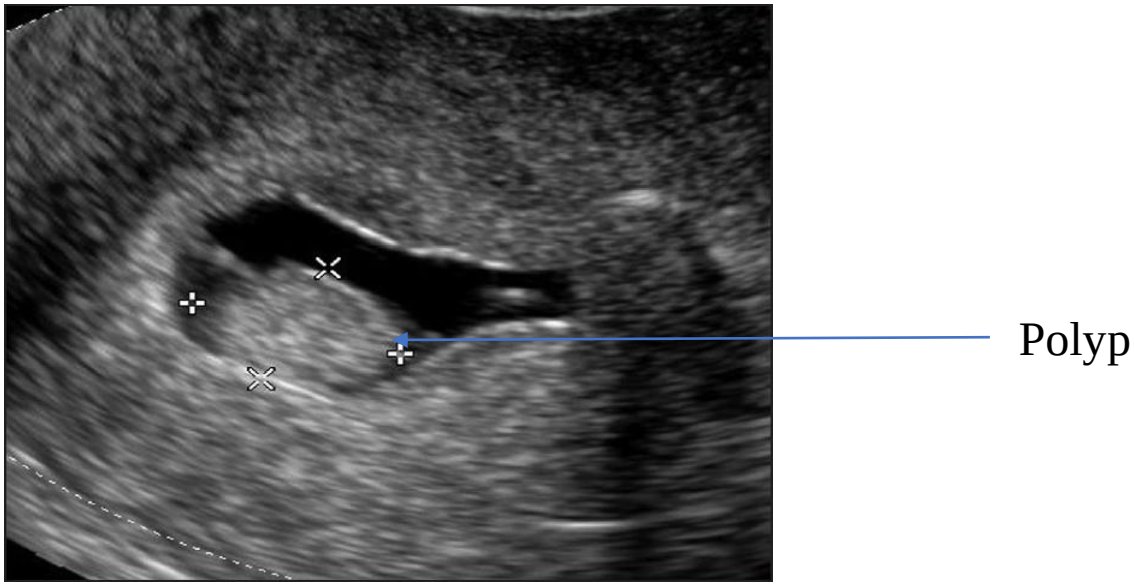


Figure 2-SIS view of endometrial polyp
(Taken from -AMA Khan F, Jamaat S, Al-Jaroudi D. Saline infusion sonohysterography versus hysteroscopy for uterine cavity evaluation. Ann Saudi Med. 2011;31(4):387–392. doi:10.4103/0256-4947.83213)

3.4.2 Hysteroscopy

This is a surgical procedure where the uterine cavity is directly examined with magnification, after distending the uterus with a suitable medium. Commonly saline is used as the distension medium while CO2 and glycerin can also be used to suit different circumstances. Procedure could be performed under anaesthesia or without anaesthesia if smaller flexible devices are used (Figure 3).

Figure 3-Flexible hysteroscope

Diagnostic procedure takes few minutes to perform and the patient can be discharged during the same day. It is generally a safe procedure; though serious complications such as uterine perforation could occur rarely. Figure 4 shows Hysteroscopic view of normal endometrial cavity (Figure 4).

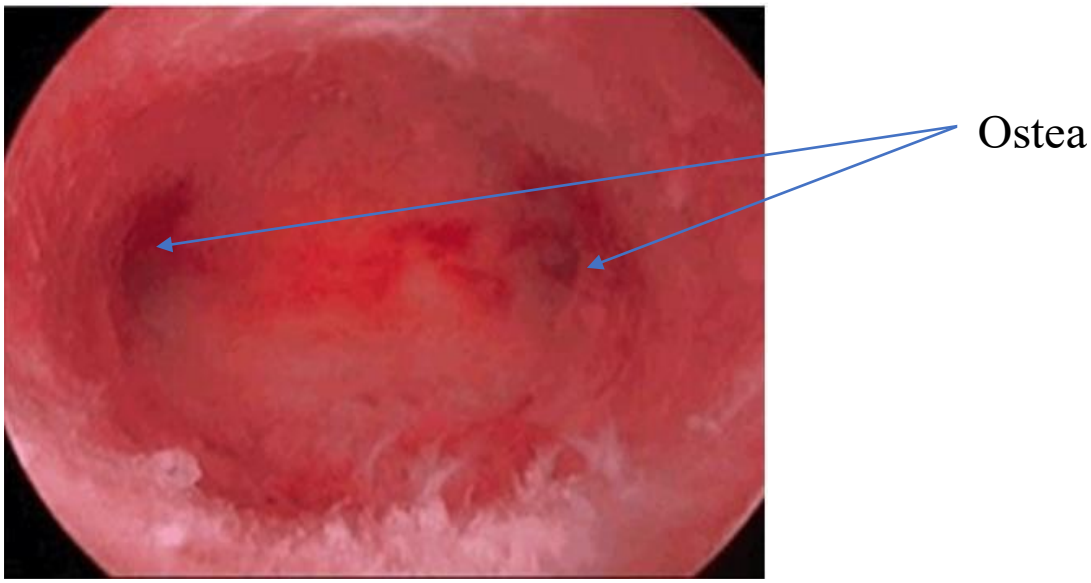


Figure 4- Hysteroscopic view of normal endometrial cavity. In this view you can clearly visualize the tubal ostea.

(Taken from- Katke RD, Zarariya AN. Use of diagnostic hysteroscopy in abnormal uterine bleeding in perimenopausal age group and its clinicopathological co-relation with ultrasound and histopathology findings: experience in a tertiary care institute. Int J Reprod Contracept Obstet Gynecol 2015;4:413-8.)

Hysteroscopy is considered as the gold standard of evaluating endometrial pathologies. An endometrial polyp is visualized as discrete outgrowth of the endometrium, attached by a pedicle, (Figure 5) which moves with the flow of the distension medium. They could be seen as pedunculated or sessile, single or multiple lesions in varying sizes and shapes. Hysteroscopy has the added advantage of allowing the operating gynaecologist to directly visualize the endometrial cavity and simultaneously carrying out a biopsy. In addition, it further allows therapeutic procedures such as removal of polyps and separation of endometrial adhesions.

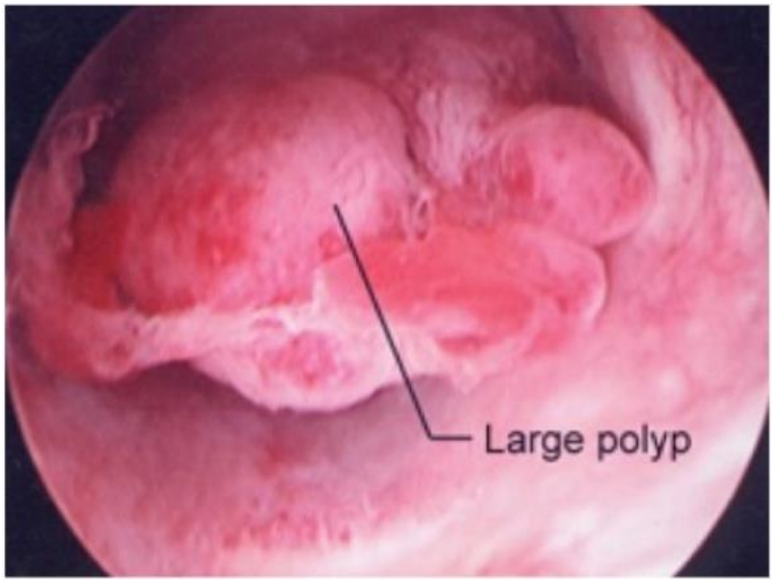


Figure 5-Hyteroscopic view of endometrial polyp
(Taken from -Katke RD, Zarariya AN. Use of diagnostic hysteroscopy in abnormal uterine bleeding in perimenopausal age group and its clinicopathological co-relation with ultrasound and histopathology findings: experience in a tertiary care institute. Int J Reprod Contracept Obstet Gynecol 2015;4:413-8.)

3.4.3 Endometrial biopsy

Endometrial biopsy provides definitive diagnosis of a polyp and enables to exclude the possibility of a malignant lesion. During the clinical examination of a women in the outpatient clinic setting, it is possible to perform an endometrial aspiration. This is a simple, cheap and relatively less uncomfortable procedure well tolerated by most woman. It is a blind procedure and may not properly sample the polyp and will not remove the polyp completely.

Traditional dilatation and curettage (D&C) is a minor surgical procedure done under general or regional anesthesia. It is technique of biopsying the endometrium blindly. The procedure leads uterine perforation during the operation which is a rare but significant complication.

These blind techniques fail to sample a significant proportion of the endometrial cavity and thus focal pathologies such as isolated uterine polyps. Therefore, they have low accuracy rate compared with hysteroscopy and guided biopsy in detecting endometrial polyps.

3.5 Treatment

3.5.1 Expectant management

The surgical treatment of endometrial polyps is excision or 'polypectomy'. Most current gynaeoclogists would offer polypectomy to their patients with a view to elevation of symptoms of AUB and arriving at a histological diagnosis. Expectant management refers to avoiding any form of treatment. This is supported by the facts that polyps are found incidentally in approximately 5-15% of women, majority being benign, some regressing spontaneously. Further some research has found control of symptoms of AUB may be equal between expectant management and surgical management groups. Therefore, it is reasonable to believe the expectant management has place among patient with minimal AUB symptoms and malignancy is unlikely possibility.

3.5.2 Medical management

There are no proven medical options to treat endometrial polyps. Hormonal options such as COCP and progestogens has been used to treat menstrual problems associated with the condition. Never the less use of the levonorgestrel-releasing intrauterine system (LNG-IUS) in women taking tamoxifen has been shown to reduce the incidence of endometrial polyps formation.

3.5.3 Surgical management

Polypectomy can be achieved by either direct visualization of the hysteroscopy for blindly.

- Blind polypectomy

Blind removal of uterine polyps during 'D&C' under general anaesthetic or avulsion with polypectomy forceps has been the common practice for decades. The technique involves adequate cervical dilatation to introduce a polypectomy forcep into the uterine cavity and explore the cavity with the hope of catching the polyp. Once the polyp is caught to in the forceps, it is twisted and avulsed. This approach could lead to uterine inversion and visceral trauma. Incomplete removal of polyps is also being well recognized complication. Most gynaecologists would perform a curettage following the procedure.

- Hysteroscopic uterine polypectomy.

Hysteroscopic technology have enabled polyps to be removed under direct vision. The procedure is performed under anaesthesia or sedation with rigid hysteroscope using a distension medium. The polyp is identified and the entire uterine cavity is explored for associated lesions. The polyp is to be removed from the stalk using mechanical scissors or electrosurgical devises. To prevent bleeding from the separation site, use of electrocautery devices will be helpful if the stalk is found to be thick. Removing the separated polyp may be difficult in situation where the polyp is large and fibrous. Use of resectoscope (electro-surgical device with a wire loop, using monopolar or bipolar current) can be used to make small chips of the polyp, that can be removed through the cervix easily. More recently different types of

tissue removal systems (TRS) has been developed to bring the specimen out of the uterus in pieces.

When suspected by ultrasound prior to IVF or prior to frozen embryo transfer (FET), polyps are usually further investigated and treated. However, the management of polyps found incidentally during the course of stimulation for IVF is controversial. Historically, it is believed that 10 % of intrauterine lesions, mainly polyps, are missed during 'blind' procedures. Therefore, hysteroscopy-directed polypectomy is recommended to minimize damage to the surrounding endometrium and to ensure the polyp has been removed in its entirety in prior to Assisted Reproductive Technique(ART).

The common occurrence of uterine polyps and its association between abnormal uterine bleeding have been documented in the International Federation of Gynecology and Obstetrics (FIGO) classification system for causes of AUB during the reproductive years. This classification uses the acronym 'PALM-COEIN' with the 'P'denoting a 'polyp'. Therefore, AUB associated with the presence of uterine polyps should be documented as AUB-P. (Figure 6).

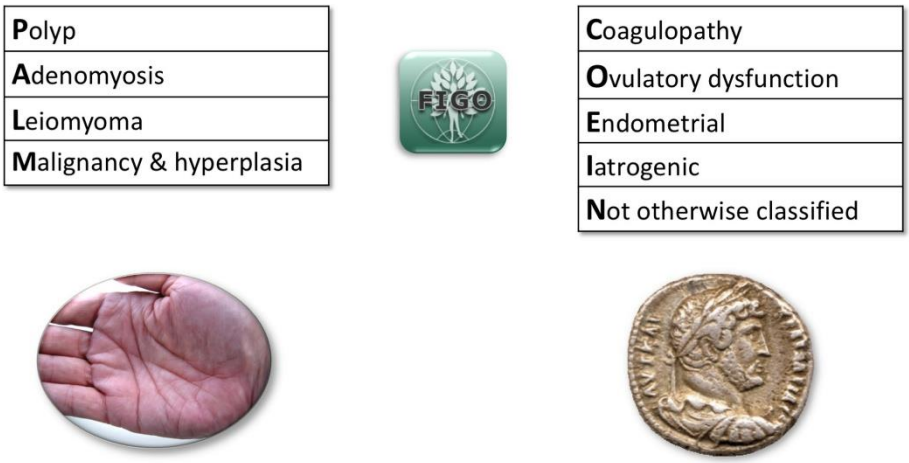


Figure 6-PALM-COEIN Classification of abnormal uterine bleeding
(Taken from-Munro MG, Critchley HOD, Fraser IS; FIGO Menstrual Disorders Committee.Int J Gynaecol Obstet. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions 2018 Dec;143(3):393-408. doi: 10.1002/ijgo.12666. Epub 2018 Oct 10. Erratum in: Int J Gynaecol Obstet. 2019 Feb;144(2):237.)

4. Fibroids

Uterine leiomyomata or fibroids are the most common benign tumours of the female genital tract, arising from neoplastic transformation of single smooth muscle cells of the myometrium. They contribute to significant proportion of women coming to our gynaecology clinics, and significant number of gynaecological surgeries.

4.1 Prevalence

They are believed to be in 70 % of women of reproductive age, and mostly remain asymptomatic, thus never diagnosed. They are very rare among pre-menarche girls and tend to regress after menopause.

There are significant racial differences in the incidence of fibroids, with Afro-Caribbean women having a two- nine fold greater risk. In addition, they tend to present at a younger age compared with Caucasian women, have multiple lesions, are more prone to both anaemia and severe pelvis.

4.2 Risk factors

As fibroids are virtually unknown among prepubertal girls and usually shrink after menopause leading to the assumption that these lesions are dependent on sex oestrogen and progesterone.

1. Age
2. Nulliparity
3. Race (Afro-Caribbean)
4. Obesity

Factors negatively associated with fibroids include increasing parity (beyond 24 weeks' gestation) and prolonged use of the oral contraceptive pill. Smoking appears to decrease the risk of fibroid development. Table 1 shows fibroids in different locations

Table 1 -Types of Fibroids according to aetiology and location

Type	Aetiology	Location
Leiomyoma	Unknown	Uterus
Parasitic	From pedunculated fibroids gaining new blood supply	Omentum, bowel
Iatrogenic	Reduced uterine blood supply (a risk with morcellation). Also reported following GnRHa and MRgFUS	Pelvis , Abdomen
Intravenous leiomyomatosis	Smooth muscle tumour emerging into the lumen of veins	Veins of the parametrium and broad ligaments
Disseminated peritoneal Leiomyomatosis	Fibroblasts replace soft peritoneal decidua on subperitoneal surfaces of the uterus and other abdominal organs	Potentially any structure within the abdomen or uterus depending on where it arises
Hereditary Leiomyomatosis and Renal Cell Carcinoma Syndrome	Autosomal dominant genetic condition	Cutaneous leiomyomas, uterine fibroids and Renal Cell Cancer

4.3 Classification

Depending on the anatomical location of the fibroids they are classified into pedunculated, intramural, submucosal, subserosal, broad ligament and cervical fibroids (Figure 7).

Fibroids closer to endometrium are called intramural while, once are in the myometrium are called intramural. Subserosal fibroids are underneath the serosa. (Figure 7 picture naming the fibroid and its location). Further they are subdivided type 0-7 depending on the closeness to the endometrium and the serosa (Table 2).

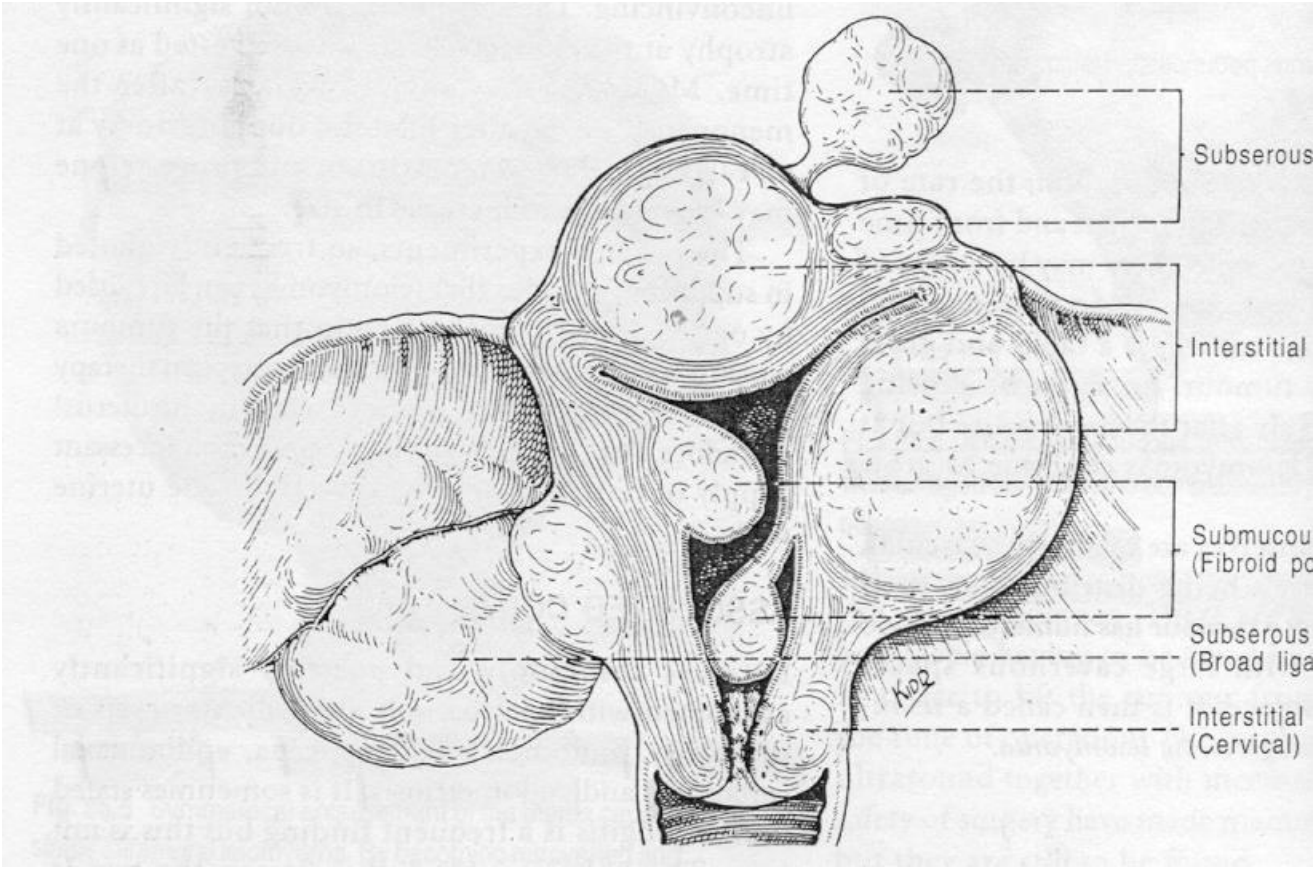
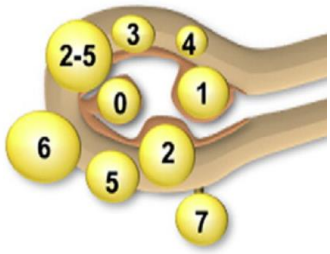


Figure 7-picture naming the fibroid and its location

Table 2-Leiomyoma sub classification system

Leiomyoma sub classification system



SM	0	Pedunculated intracavitary
	1	<50% intramural
	2	>= intramural
O-Other	3	Contacts endometrium;100% intramural
	4	intramural
	5	Subserosal >= intramural
	6	Subserosal <50%intramural
	7	Subserosal pedunculated
	8	Other(specify e.g.cervical,parasitic)
Hybrid leiomyomas (impact both endometrium and serosa)	Two numbers are listed separated by a hyphen. By convention, the first refers to the relationship with the endometrium while the second refers to the relationship to the serosa. One example is below.	
	2-5	Submucosal and subserosal, each with less than half the diameter in the endometrial and peritoneal cavities,repectively.

Intracavitary lesions are attached to the endometrium by a narrow stalk and are classified as type 0, whereas types 1 and 2 require a portion of the lesion to be intramural; with type 1 being less than 50% and type 2 at least 50%. The type 3 lesions are totally extracavitary but abutting the endometrium. Type 4 lesions are intramural leiomyomas that are entirely within the myometrium, with no extension to the endometrial surface or to the serosa. Subserosal (types 5–7) leiomyomas represent the mirror image of the submucosal leiomyomas—with type 5 being at least 50% intramural, type 6 being less than 50% intramural, and Type 7 being attached to the serosa by a stalk. Classification of lesions that are transmural would be categorized by their relationship to both the endometrial and the serosal surfaces. The endometrial relationship would be noted first, with the serosal relationship second (e.g. 2-3). An additional category, Type 8, is reserved for leiomyomas that do not relate to the myometrium at all, and would

include cervical lesions, those that exist in the round or broad ligaments without direct attachment to the uterus, and other so-called "parasitic" lesions.

4.4 Histology / Pathology

Fibroids are benign monoclonal tumours that arise from the uterine smooth-muscle tissue. They are spherical, firm and commonly multiple. They have a pseudo-capsule and can be easily enucleated. Fibroids are paler than the surrounding myometrium and there is usually a very sharp line of demarcation between the tumour and the normal uterine muscle. The cut surface, which bulges out and has whorled appearance.

The reasons fibroids develop and grow are not well understood, but many factors are recognized as growth promoters, such as sex steroids, oestrogen and progesterone, being the most frequently studied

Degeneration occurs when there is insufficient blood supply, and especially in rapidly growing fibroids. "Red degeneration" is characteristic in pregnancy and is due to acute infarction, with a prevalence of 1-10%. It is a painful condition that subside spontaneously. Almost 2/3 of all fibroids, not only in pregnancy, show some degree of degeneration. When the degenerated tissue is replaced with fibrous tissue, it is called "hyaline degeneration." This phenomenon is reported in 65% of the cases, followed by myxomatous degeneration, calcification, and rarely cystic and fatty degeneration.

It is reported that 20-50 % fibroids will remain asymptomatic.

Table 3-Clinical presentations / problems due to fibroids

Presentations / Problems due to fibroids	**Possible explanation**
Menstrual problems	
Heavy menstrual bleeding	Presence of surface vessels and larger surface area of the endometrium created by submucosal fibroids
Intermenstrual bleeding	Specially fibroid polyps, infected sloughing surface cause intermenstrual bleeding
Pain associated with periods	As the uterus is trying to expel fibroid polyps in the uterine cavity
Pressure/ Obstructive problems symptoms	
Bowel symptoms	
Ureteric compression	Fibroids growing into the broad ligament are likely to cause ureteric obstruction as it can compress the fibroid on to the lateral pelvic wall
Over stretching of urethra	Cervical fibroids may lead to acute retention of urine due to urethral obstruction
Dragging sensation, feeling of pressure in the pelvis, abdominal swelling	Size of the fibroid
Incomplete emptying of the bladder	Cervical fibroid may over stretch the urethra and cause incomplete emptying

urinary incontinence	Increase intra-abdominal caused by large fibroids
Constipation	Fibroids that develop in the back of the uterus can press on the colon from the outside,
Fertility related problems	
Failure if implantation	Submucosal fibroids, and intramural fibroids, which are closer to the endometrium
Recurrent miscarriage	Mechanical distortion of the cavity
Tubal factor infertility	Cornual fibroids may block the tubes
Pregnancy / Labour related problems	
Pain during pregnancy	Due to red degeneration of the fibroids
Small for Gestational Age	Once the placenta is attached on to the fibroid, it will receive relatively less blood supply
Malpresentations	Large lesions occupying the pelvis will prevent the presenting part to engage into the pelvis
Labour dystocia /lack of progress	Intramural fibroids would cause incordinated uterine activity
Higher Caesarean Section rate	Due to incordinated contractions and malpresentations
Postpartum haemorrhage	Larger bleeding surface area, Retraction of the uterus is impaired due to the fibroid,
Postpartum endometritis	Due to increase surface area
Miscellaneous issues	
Polycythaemia	intra-uterine shunting; compression of the ureters, resulting in inappropriate excessive production of erythropoietin by the kidneys; tissue hypoxemia in the myomata, causing increased polycythaemia, increased erythropoietin production or erythropoietin-like substance from the myomatous tissue; or increased life span of the red blood cells.
Malignant transformation	Whether a causative or association is still unclear
Parasitic fibroids	accidental seeding during morcellation of uterine fibroids for removal during surgery

The location of the fibroids is being used by the FIGO for the classification of fibroids. The common occurrence of fibroids and its association between abnormal uterine bleeding have been documented in the International Federation of Gynecology and Obstetrics classification system for causes of AUB during the reproductive years. This classification uses the acronym 'PALM-COEIN' with the 'L'denoting a 'leiomyoma'. Therefore, AUB associated with the presence of uterine polyps should be documented as AUB-L

4.5 Diagnosis

The physical signs a fibroid could produce depends on the size and the location. Small type 0-3 fibroids may not be detectable clinically. Larger uteri are palpable abdominally, and felt as a firm, nontender mass with regular margins and a smooth surface. Broad ligament fibroids are felt as adnexal masses during vaginal examination, while cervical fibroids could be felt as distorted cervix or polyps.

During surgery, fibroids are diagnosed on the basis of the macroscopic features described in the pathology section (Figure 8).

Figure 8a- Macroscopic view of a fibroid uterus

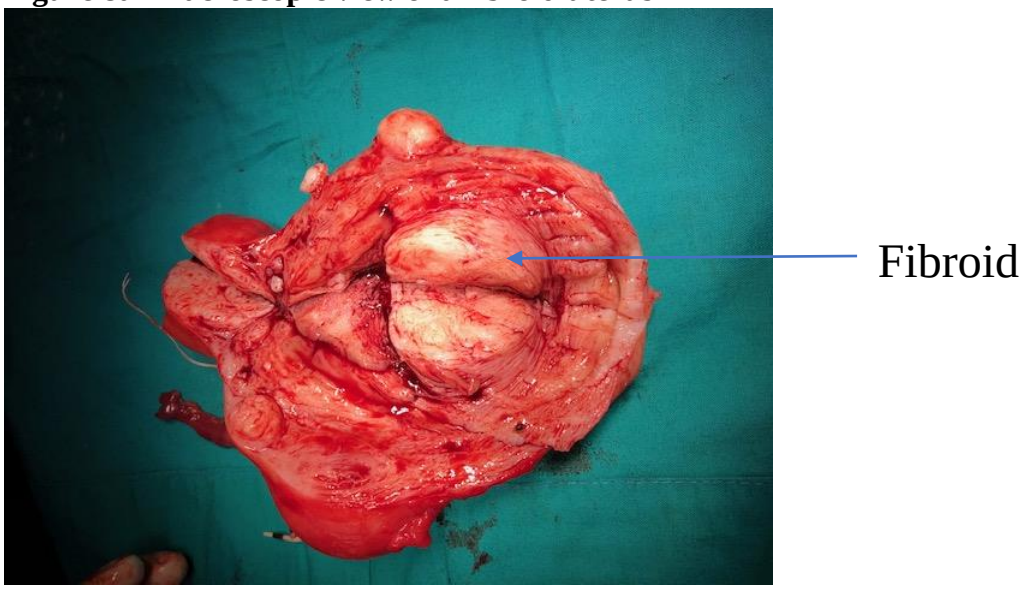


Figure 8b-Cut section of uterus with multiple fibroids

4.5.1 Imaging

Ultrasonography is useful as a the first-line diagnostic test. Fibroids are typically well-defined round or lobulated myometrial lesions. The echogenicity is highly variable: it may be uniform hypoechogenic, isoechogenic or hyperechogenic as compared with the surrounding myometrium, or non-uniform due to mixed echogenicity, internal hyperechogenic spots or calcifications. These calcifications may cause intense shadowing. On colour Doppler a fibroid typically has circumferential vascularization, and sometimes some internal vascularization too. Ultrasonography can also be used to describe the relationship of the fibroid to the endometrial cavity (Figure 9).

Figure 9-Ultrasnographic view of fibroid

It is important to look for complications like hydroureter and hydronephrosis in cases of large fibroids as they can obstruct the ureters.

MRI is useful for examining large fibroids or in obese women where adequate imaging on transvaginal or transabdominal ultrasonography is precluded, or in cases of suspected malignancy. There are no pathognomonic features for identifying leiomyosarcoma on any imaging technique Figure 10. (MRI images of Fibroids)

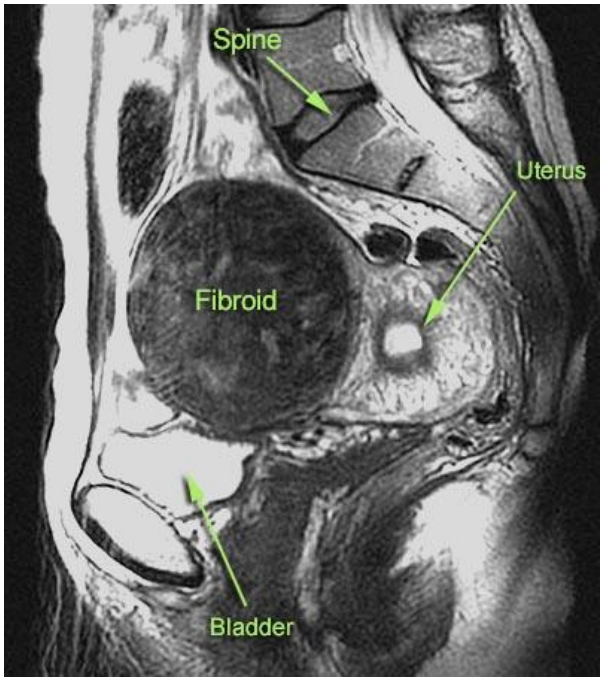


Figure 10-MRI view of fibroid

4.6 Treatment

Most fibroids remain asymptomatic and will never be diagnosed. The treatment will basically depend on the degree of symptoms/complications and the fertility wishes of the patient.

Management of asymptomatic fibroid involves considerable controversy and uncertainty. This is often the case when the presence of a small fibroid <5 cm is a concomitant pathology with a fertility problem. The injury to the myometrium and the risk of postoperative adhesion formation when removing even a small intramural fibroid, raises serious concerns.

Usually, asymptomatic fibroids without any suspicion of malignancy, diagnosed incidentally while routine ultrasound scans are expectantly managed until menopause. After menopause, the fibroid will eventually decrease in volume because of oestrogen deprivation. If HRT is commenced, then the size and characteristics of the fibroid should be evaluated and results discussed with the patient as the progression, growth and symptoms will be unpredictable.

4.6.1 Medical management

Non-hormonal treatment

- Non-steroidal anti-inflammatory drugs

Medications like mefenamic acid, ibuprofen and naproxen has been used to treat AUB and menstrual pain associated with fibroids. NSAIDs were found to be superior to placebo but less effective than tranexamic acid, danazol, or the levonorgestrel releasing intrauterine device when evaluating the therapeutic impact on abnormal uterine bleeding. Further, these agents do not have any effect on the size of the leiomyoma.

- Tranexamic acid

Tranexamic acid is an anti-fibrinolytic agent that prevents fibrin degradation by competitively blocking lysine-binding sites on plasminogen, thereby preventing fibrin degradation. This action favors clotting, thus reducing menstrual blood flow. Several randomized control trials have demonstrated a reduction in menstrual blood flow as compared to placebo. Despite the symptom control it archives in women with uterine leiomyomata, tranexamic acid has no effect on reducing the burden of disease.

Medical – Hormonal treatment

- Combined oral contraceptive pill

The combined contraceptive pill contains both oestrogens and progestrogens and hence called combined oral contraceptive pill(COCP). COCP has been used to reduce menstrual bleeding in women with fibroids. As uterine fibroid growth is stimulated by both oestrogens and progestogens, COCP were considered a risk factor for fibroid growth in the past. However, a recent meta-analysis suggests that uterine fibroids should not be considered a contraindication for COCP use. Therefore, COCP can be used to improve heavy menstrual bleeding associated with fibroids, primarily through their suppressive effects on endometrial proliferation. But they have no proven effect on decreasing fibroid volume or uterine size.

- Progestogens

Progesterone containing oral, injectable, and implantable contraceptives act to reduce blood loss by providing an inhibitory effect on endometrial cell proliferation leading to a thinner lining with less material to be shed during progestin withdrawal. Treating uterine fibroids with progestogens has been effective in some cases, but such treatment has been associated with histopathological changes that may be mistaken for leiomyosarcoma or smooth-muscle tumors of unknown malignant potential, such as an increase in cellularity and mitotic activity. There is no evidence about the effect of such treatment on the size of the fibroid.

- LNG- IUS

Levonorgestrol releasing intrauterine systems (LNG-IUS) are effective at treating abnormal uterine bleeding associated with anovulation. The levonorgestrel releasing intrauterine system acts at the level of the endometrium to suppress estrogenic effect, and thinning it out to minimize menstrual bleeding. This has been used successfully in situations of AUB due to fibroids in small clinical studies.

LNG-IUS can be used for the symptoms of menorrhagia if the fibroid is non-submucosal and small fibroid (Figure 11).

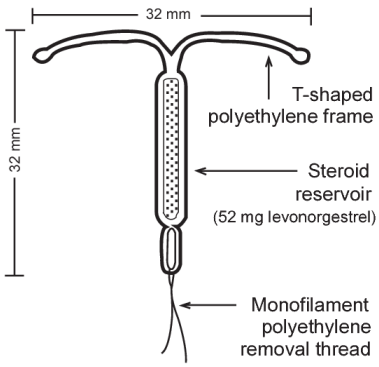


Figure 11- Levonorgestrol releasing intrauterine system

- Aromatase inhibitors

Aromatase is an enzyme responsible for ovarian and peripheral conversion of androgens, namely, testosterone, to estradiol. In vitro studies demonstrated that uterine leiomyoma cells carry intrinsic aromatase activity, thereby providing a self-propagated source of steroid hormone to drive their growth through the development of an aberrant extracellular matrix. Based on this argument, aromatase inhibitors were hypothesized to shrink the fibroid with minimum side effects. To current data there is no strong evidence to use aromatase inhibitors as a treatment.

- GnRH agonists

GnRH is a hypothalamic hormone, released in pulsatile nature, and directly controls the release of gonadotrophins from the pituitary. GnRH agonists occupy the GnRH receptor in the pituitary, preventing being exposed to pulsatile nature of the hypothalamic GnRH. This leads to hypo-gonadotrophic status resulting in reduced circulating estrogen levels, thus making the fibroid smaller. The downregulation of the hypothalamic-pituitary-ovarian axis leads to amenorrhea, improvement in menstruation related symptoms (namely, AUB-HMB/IMB), and rapid reduction in leiomyomata volume. Studies have shown that approximately 30–65% of reduction of leiomyomata volume can be achieved by using GnRH agonist over a period of 6 months. In clinical practice it is used to for symptom control prior to surgical interventions. GnRh agonists have been proven to reduce pre-operative blood transfusions, and the need for making midline incisions during myomectomy for large fibroids fibroid

The benefits from GnRH agonist come with an unavoidable cost; symptoms due to hypo-estrogenic status include vasomotor symptoms, vaginal dryness, sleep disturbances, myalgia, arthralgia, mood-swings, and potential cognitive impairment. Long-term therapy, greater than 6 months, with GnRH agonists has been shown to cause a bone loss of approximately 6%.

Therefore, the use of GnRH has been limited for symptomatic women scheduled to undergo surgery within 6 months of initiating therapy. If longer regimens are used, low dose steroidal add-back therapy need to be considered to minimize bone loss and vasomotor symptoms. It is imperative to emphasize that side effects, of GnRH agonists are temporary and reverse with the discontinuation of the medication.

- GnRH antagonist

Similar to the GnRH agonists, GnRH antagonists have been shown in trials to shrink the fibroid volume via induction of a hypoestrogenic state. However, these medications are injected and must be taken once in 1 to 4 days limiting their usefulness in the treatment of leiomyomata.

- Antiprogestins.

Progesterone receptor A and B (PR-A, PR-B) protein has been implicated in growth of fibroids as they are found to be in abundance within leiomyomata, as compared to adjacent myometrium. These make suppression of progesterone receptor a possible treatment of medical management of leiomyomata.

Mifepristone, also known as RU 38486 & RU486, is the most extensively studied progesterone receptor antagonist in leiomyomata. A Cochrane review evaluated the usefulness of mifepristone for symptomatic leiomyomata. It concluded mifepristone reduced heavy menstrual bleeding/ intermenstrual bleeding, and also improved fibroid specific quality of life. Despite the improvement of symptoms, the Cochran review found no significant reduction in leiomyomata volume with mifepristone therapy. Though the improvement of symptoms achieved my antiprogestins without the side effects of GnRH, the main concern is that it exposes the endometrium to unopposed estrogenic activity predisposing to endometrial hyperplasia. Therefore, antiprogestins should be used with caution as it has the theoretical possibility of development of endometrial malignancy and this remains the main limitation to its use.

- Selective progesterone receptor modulators (SPRMS)

Progesterone has been implicated in the growth of the fibroids in vitro and in vivo studies. In vitro studies demonstrate that progesterone stimulates proliferative activity in cultured uterine fibroid cells, but not in normal myometrial cells. A number of clinical observations also support these observations. The use of progestins in hormone-replacement regimens stimulates the growth of fibroids in postmenopausal women in a dose-dependent manner. Further, addition of progestins as add-back therapy to GnRH agonists diminishes the inhibitory effects of these agonists on uterine fibroid size. Therefore, it is considered Progesterone is essential for fibroid growth, and these observations have led the way for development of progesterone antagonist and/or Selective progesterone receptor modulators (SPRM) drugs.

SPRMs have tissue-specific agonist and antagonist effects on progesterone receptors (PR), making useful in the treatment of uterine leiomyomata. Members of this class of medication are telapristone acetate, asoprisnil and ulipristal acetate (UPA), and ulipristal being the mostly tested SPRM.

UPA is a synthetic steroid derived from 19-norprogesterone, which is a selective PR modulator that binds to PR-A and PR-B with high affinity. The binding and antagonist potency of UPA with the glucocorticoid receptor is significantly reduced compared to mifepristone. UPA is tissue selective, with preferential binding noted to uterine, cervical, ovarian, and hypothalamic receptors.

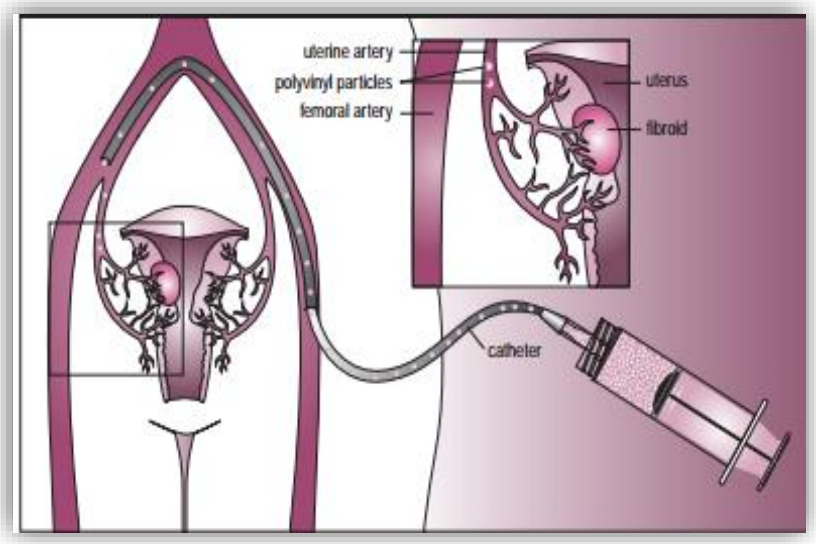
UPA has been shown to reduce AUB >80% of women after 3 months of use and reduce the size of fibroids by 58%, and restore quality of life. It is not being associated with the

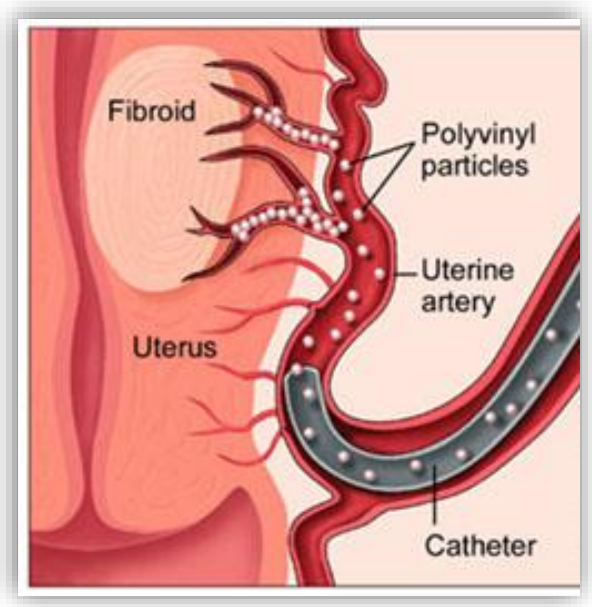
development of endometrial hyperplasia with atypia or endometrial malignancy as seen with antiprogestogens, probably due to UPA's selective activity. Nevertheless, non-physiologic endometrial changes characterized by dilated weakly secretory endometrial glands with few mitotic figures, and stromal effects ranging from compaction to nonuniform edema have been described, which have been termed "progesterone receptor modulator-associated endometrial changes (PAECs). PAECs occur in approximately 50% of all patients and known to be reversible after cessation of UPA.

Based on these advantages, UPA administration has been identified as feasible conservative treatment options for uterine fibroids.

- Uterine artery embolization (UAE)

UAE is a radiological intervention intended to devascularize the uterine arteries by embolising the uterine arteries. During the procedure, a catheter through femoral arteries is introduced to reach uterine arteries and microscopic particles are injected into them, resulting in occlusion and devascularization of the vessels. This will eventually lead to an infarction and atrophy of the fibroid (Figure 12).





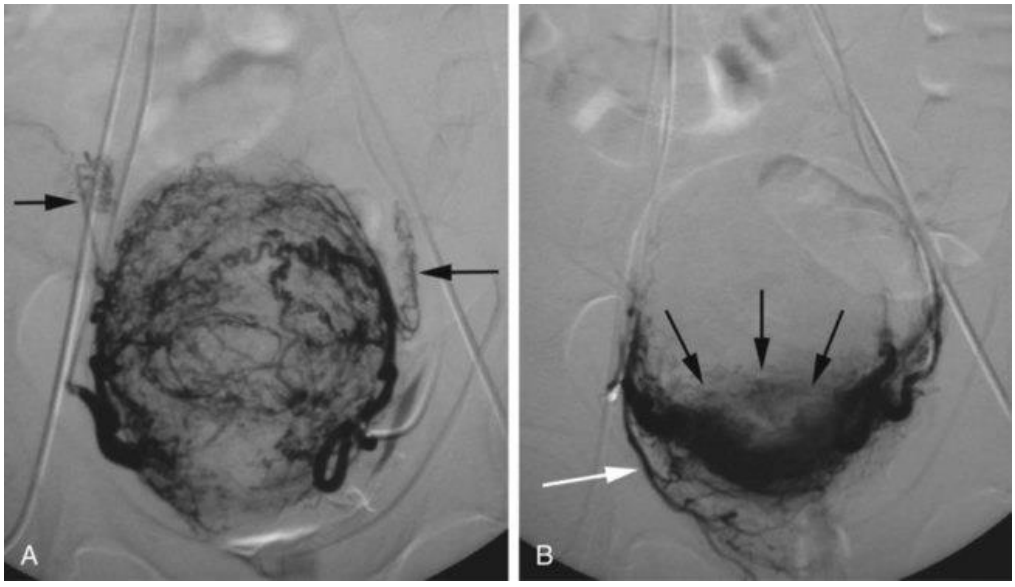


Figure 12-Uterine artery embolization

This procedure is useful for single fibroids or fibroids that are less than 10 cm in diameter and in uteri less than the size at 20 weeks' gestation. The re-intervention rate is higher compared to in myomectomy, however, and myomectomy may still be recommended over UAE for patients with infertility concerns.

UAE has many advantages to women seeking non-surgical interventions including preservation of the uterus, fewer surgical complications, avoidance of general anesthesia, and significantly quicker recovery period.

Clinical outcomes following UAE are encouraging. UAE has been proven to improve quality of life, improvement in physical and emotional fibroid-related symptoms, improvement in

bleeding (79%), pain (82%), bulk-related symptoms, urinary dysfunction, sexual dysfunction, fatigue, limitations in social life in and depressed mood.

Mean uterine and dominant fibroid volumes were reduced by 55% and 73% using ultrasound at an average of 9.7 months and 53% and 64% using MRI at an average of 6.4 months.

The main disadvantage of UAE is the potential for fibroid recurrence (estimated to be 5 % per year and as high as 28% after 5 years) which is a result of incomplete fibroid infarction.

UAE is associated with increased risk of miscarriage and preterm labour in subsequent pregnancy and is not recommended for women planning a pregnancy. Given the lack of robust data, the counseling of women considering fertility following UAE should be individualized. When the fibroid is amenable to myomectomy and the patient desires future pregnancy, then surgery should be the first recommended procedure. If the patient's anatomy is not suitable for surgery, then UAE should be offered as therapy.

4.6.2 Surgical management

Hysterectomy and myomectomy remains the main treatment option for women with symptomatic fibroids. Traditionally if the family is completed in women over 40 years, hysterectomy is recommended where the symptoms are troublesome. Hysterectomy can be done as an open surgery or with the laparoscopic route. Using minimal access method such as laparoscopic hysterectomy would allow the women to recover faster and to have a better cosmetic outcome. However, size of the fibroid uterus and the operator's expertise are important determinants of the route of the surgery. If the fibroid uterus is large it occupies a large space in the abdominal cavity making it difficult for a laparoscopic surgery.

- Myomectomy

Myomectomy refers to surgical removal of the fibroid and it can be achieved with either open surgery, laparoscopically or hysterescopically. Submucosal fibroids (FIGO group 0,1,2) which are < 4cm can be resected hysteroscopically. In women concern about fertility, laparoscopic myomectomy is preferred as this approach is known to reduce post-surgical adhesions, which could implicate future fertility. In cases of women aged between 35 and 40 years where there is uncertainty about future child bearing, still laparoscopic myomectomy is recommended.

Myomectomy is a surgically demanding procedure which involve removal of fibroids, repair of the uterus in a way to be able to bear a pregnancy later, and minimising formation of pelvic adhesions. As the fibroid has a vascular pseudo-capsule, myomectomy presents a risk of primary haemorrhage. Lager and multiplicity of fibroids leave a large surface area of pseudo-capsule exposed predisposing to haemorrhage.

Laparoscopic myomectomy is the approach of choice if fertility is required. Large fibroids, and if there are multiple fibroids open surgery is preferred. It is likely that small seedling fibroids are missed during laparoscopic myomectomy, as theses cannot be felt, in contrast to open surgery. One of the main problems of laparoscopic myomectomy is removing the specimen

out of the abdominal cavity. Morcellation is a procedure that is used to remove the fibroid from the abdominal cavity, with the help of device which cuts it to small pieces.

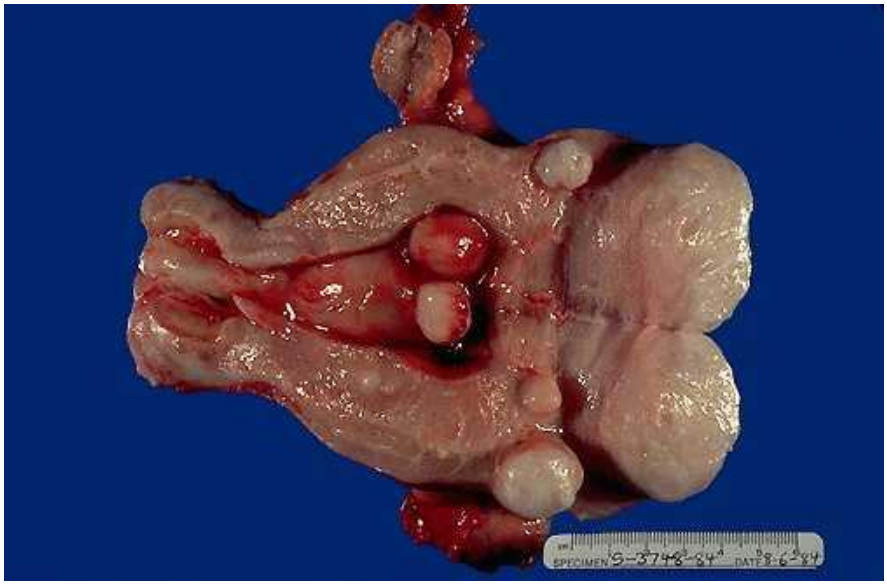
Achieving haemostasis is of paramount importance after fibroid enucleation. Use of diathermy targeting only the vessels and suturing the raw area will help achieving haemostasis. The damage to healthy myometrium should be minimized during the surgery as it will hamper healing. Injection of ADH (vasopressin derivative solutions) or diluted adrenalin around the fibroid wall (extracapsular) causes blood vessels to constrict and minimizes the bleeding during dissection. Similarly, temporary bilateral uterine artery clipping reduces the blood supply and bleeding during myomectomy.

Video 1- Laparoscopic myomectomy

Video 2 -Hysteroscopic myomectomy

Complications of myomectomy

Complications of general anaesthesia
Complications of any open abdominal surgery
Complications of laparoscopic surgery
Complications of myomectomy
Haemorrhage (primary, reactionary, secondary)
Pelvic adhesions (leading to pelvic pain, difficulties in subsequent surgery, fertility issues)
Scared uterus (and associated implications in subsequent pregnancy)
Recurrence of fibroids (women undergo myomectomy will require a subsequent surgery for fibroids in 9% of cases)
Complications of morcellation (seedling of fibroids in the abdominal cavity)



5. Case discussion

38 years old nulliparous lady presented with a history of primary subfertility for 4 years. She also complained of heavy menstrual bleeding for 1 year, which increased in severity with time and her menstruation became irregular. She does not have symptoms of anaemia. She was admitted to the ward for Laparoscopic myomectomy.

Her menarche was at 16 years of age and since then she had regular cycles until she became symptomatic one year back. She never had significant pain during menstrual periods. She is a known patient with hypothyroidism with a regular clinic follow up and she is on Thyroxine 50 µg in the morning. Her last TSH (Thyroid Stimulating Hormone) value which was done a week before is within the normal range. She does not give any symptoms of hypothyroidism. She underwent a laparoscopy and dye test in 2016 which did not reveal any abnormality. She does not give a history of any food medication or plaster allergies. She does not have any significant family history of illnesses.
She is a graduated School teacher who is married to an engineer. She is having a very good family support and her awareness about her condition is satisfactory.

Her BMI was 28 Kg/m^2. Her general and systemic examination was unremarkable.
Abdominal examination revealed a pelvic mass of 16 weeks of a gravid uterus. It was firm and non-tender. It had regular margins and smooth surfaces. Uterine cervix was healthy and no bleeding or discharges found on speculum examination. Bi manual examination revealed the pelvic lump to be originated from uterus and there were no adnexal masses.

Investigations

- Ultrasonography of the abdomen and pelvis (Figure 13) was performed as a part of her investigations.

Findings
Uterus anteverted and enlarged with a fundal submucosal fibroid 5cm × 6cm in size and intramural fibroid 3cm × 3 cm in size noted on the posterior wall.
Endometrial thickness is 6mm. Bilateral ovaries appear normal. No pelvic masses. No free fluid. Rest of the Ultrasound scan was normal.

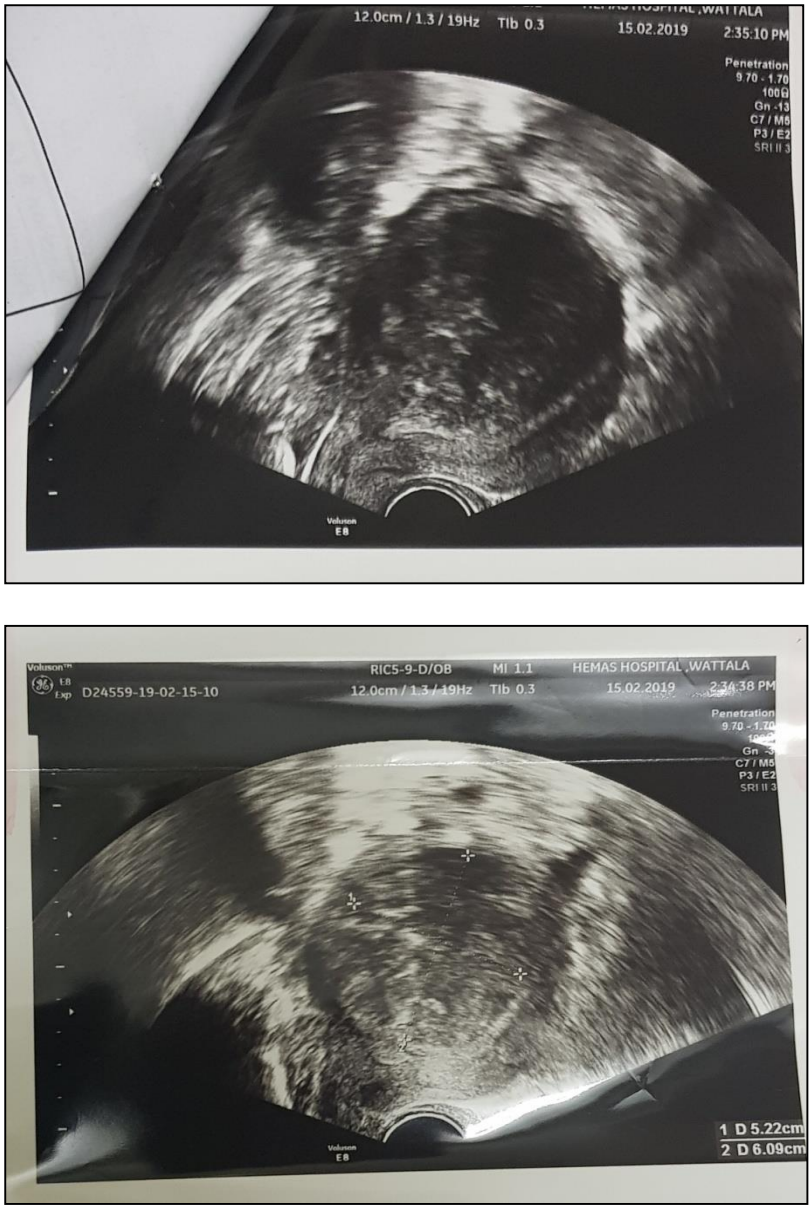
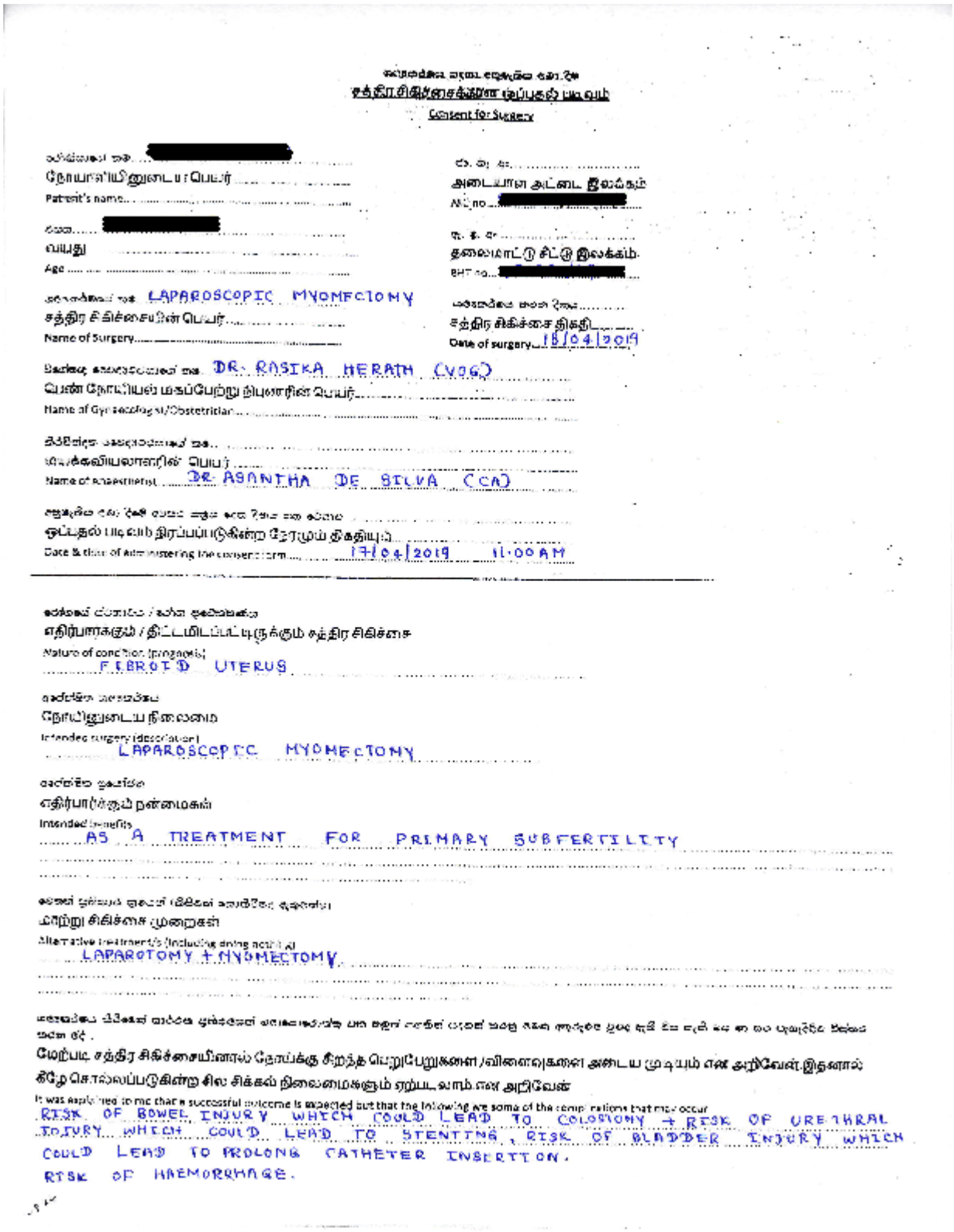


Figure 13-Ultrasonography of the abdomen and pelvis

- Full blood count (FBC)
- Prothrombin time (PT)
- Activated partial thromboplastin time (APTT)

Patient underwent laparoscopic myomectomy. Consent form, Full blood count, prothrombin time, thyroid function test, request form for red cell products, operation note and pathology request form are below.

5.1 Consent form



சத்திர சிகிச்சைக்கான ஒப்புதல் படிவம்

Consent for Surgery

[redacted]

நோயாளியினுடைய பெயர்

Patient's name

[redacted]

அடையாள அட்டை இலக்கம்

NIC no [redacted]

[redacted]

வயது

Age

[redacted]

தலைமாட்டு சீட்டு இலக்கம்

BHT no [redacted]

சத்திர சிகிச்சையின் பெயர் LAPAROSCOPIC MYOMECTOMY

Name of Surgery

சத்திர சிகிச்சை திகதி

Date of surgery 18/04/2019

பெண் நோய்யியல் மகப்பேற்று நிபுணரின் பெயர் DR. RASIKA HERATH (CO&G)

Name of Gynaecologist/Obstetrician

மயக்கவியலாளரின் பெயர் DR. ASANTHA DE SILVA (CCA)

Name of Anaesthetist

ஒப்புதல் படிவம் நிரப்பப்படுகின்ற நேரமும் திகதியும் 17/04/2019 11.00AM

Date & time of administering the consent form

எதிர்பார்க்கும் / தீர்மானிக்கப்பட்டிருக்கும் சத்திர சிகிச்சை

Nature of condition (prognosis)

FIBROID UTERUS

நோயினுடைய நிலைமை

Intended surgery (description)

LAPAROSCOPIC MYOMECTOMY

எதிர்பார்க்கும் நன்மைகள்

Intended benefits

AS A TREATMENT FOR PRIMARY SUBFERTILITY

மாற்று சிகிச்சை முறைகள்

Alternative treatments (including doing nothing)

LAPAROTOMY + MYOMECTOMY

மேற்படி சத்திர சிகிச்சையினால் நோய்க்கு சீறைத்த பெறுபேறுகளை/விளைவுகளை அடைய முடியும் என தெரிவேன் இதனால் கீழே சொல்லப்படுகின்ற சில சிக்கல் நிலைமைகளும் ஏற்படலாம் என அறிவேன்

It was explained to me that a successful outcome is expected but that the following are some of the complications that may occur

RISK OF BOWEL INJURY WHICH COULD LEAD TO COLOSTOMY + RISK OF URETHRAL INJURY WHICH COULD LEAD TO STENTING, RISK OF BLADDER INJURY WHICH COULD LEAD TO PROLONG CATHETER INSERTION.

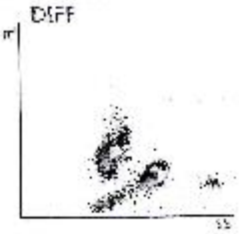
RISK OF HAEMORRHAGE.

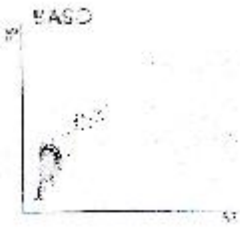
5.2 Full blood count

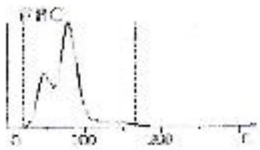
Colombo North Teaching Hospital

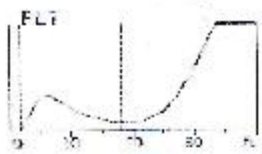
First Name:	[redacted]	Last Name:		Sample ID:	126
Gender:		Age:		Patient ID:	[redacted]
Department:		Bed No.:		Date of Analysis:	4/25/2019 12:59 PM
Mode:	AL-WB-CD				
Diagnosis:					

Para.	Flag	Result	Unit	Ref. Ranges
WBC		**6.80**	**10^3/uL**	**4.00 - 10.00**
Neu#		4.37	10^3/uL	2.00 - 7.00
Lym#		2.08	10^3/uL	1.00 - 3.00
Mon#		0.25	10^3/uL	0.12 - 1.20
Eos#		0.08	10^3/uL	0.02 - 0.50
Bas#		0.02	10^3/uL	0.02 - 0.10
Neu%		64.2	%	50.0 - 70.0
Lym%		30.6	%	20.0 - [illegible]
Mon%		3.6	%	3.0 - 12.0
Eos%		1.2	%	0.5 - 5.0
Bas%		0.4	%	0.0 - [illegible]
RBC		4.62	10^6/uL	4.00 - 5.50
HGB	**L**	**11.2**	**g/dL**	**13.2 - 16.5**
HCT	**RL**	**34.5**	**%**	**36.0 - 47.0**
MCV	RL	74.6	fL	80.0 - 100.0
MCH	L	24.2	pg	27.0 - 34.0
MCHC	R	32.5	g/dL	32.0 - 36.0
RDW-CV	RH	27.8	%	11.0 - 16.0
RDW-SD	RH	73.0	fL	35.0 - 56.0
PLT		**222**	**10^3/uL**	**150 - 400**
MPV		8.8	fL	6.5 - 12.0
PDW		[illegible]		15.0 - 17.0
PCT		0.195	%	0.108 - 0.282
P-LCC		48	10^9/L	30 - 90
P-LCR		21.6	%	11.0 - 45.0
IMG#		0.00	10^9/L	0.00 - 999.99
IMG%		0.000		0.000 - 1.000









Delivered by:
Order Time:
Comments:

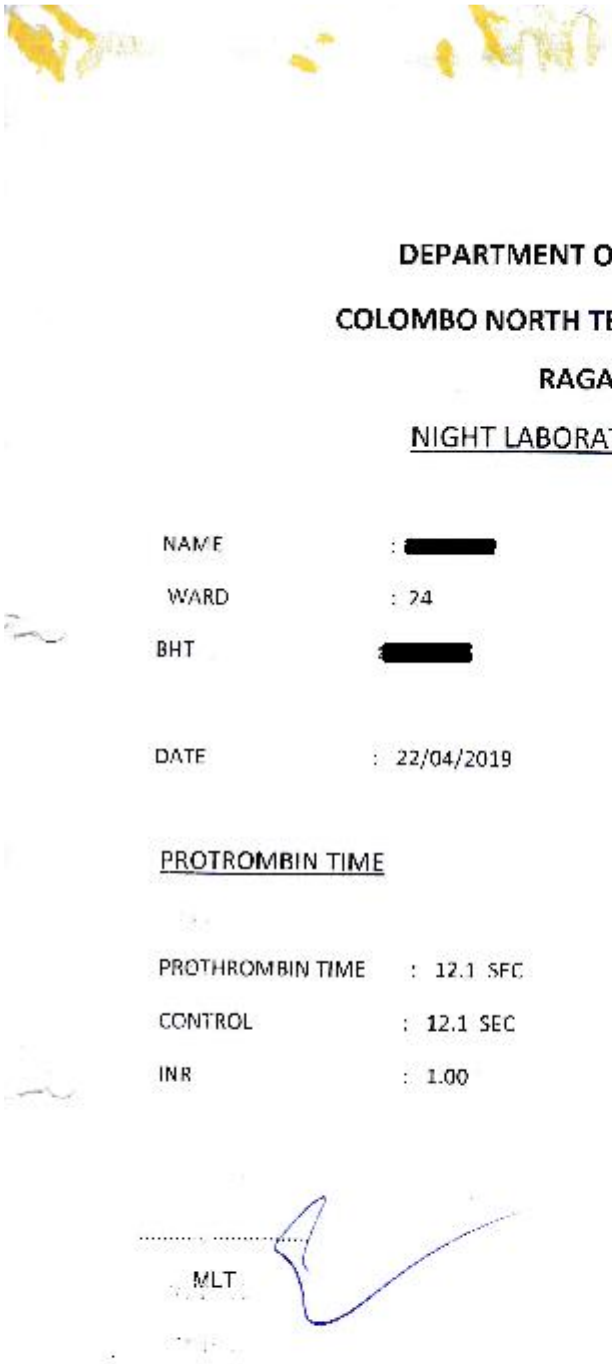
Operated by: MLT
Draw Time:

Validated by:
Time of Printing: 4/25/2019 12:59:57 PM

[The analysis result is only answer to the corresponding sample]

1 / 1

5.3 Prothrombin time



DEPARTMENT OF PATHOLOGY

COLOMBO NORTH TEACHING HOSPITAL

RAGAMA

NIGHT LABORATORY REPORT

NAME : [redacted]

WARD : 24

BHT [redacted]

DATE : 22/04/2019

PROTROMBIN TIME

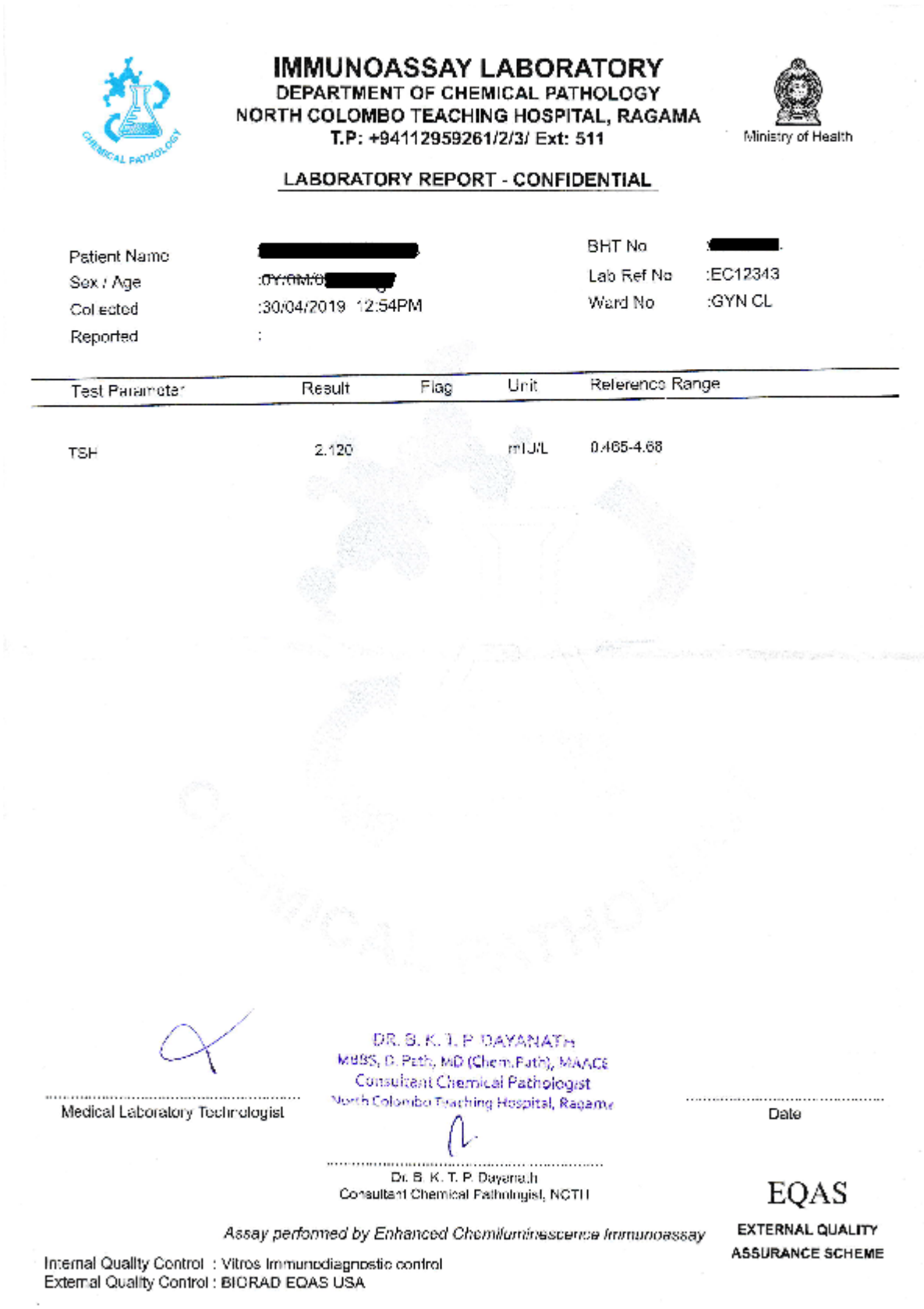
PROTHROMBIN TIME : 12.1 SEC

CONTROL : 12.1 SEC

INR : 1.00

MLT

5.4 Thyroid function test



IMMUNOASSAY LABORATORY
DEPARTMENT OF CHEMICAL PATHOLOGY
NORTH COLOMBO TEACHING HOSPITAL, RAGAMA
T.P: +94112959261/2/3/ Ext: 511

Ministry of Health

LABORATORY REPORT - CONFIDENTIAL

Patient Name	[redacted]	BHT No	[redacted]
Sex / Age	:[redacted]	Lab Ref No	:EC12343
Collected	:30/04/2019 12:54PM	Ward No	:GYN CL
Reported	:		

Test Parameter	Result	Flag	Unit	Reference Range
TSH	2.120		mIU/L	0.465-4.68

DR. S. K. T. P. DAYANATH
MBBS, D. Path, MD (Chem.Path), MAACB
Consultant Chemical Pathologist
North Colombo Teaching Hospital, Ragama

Medical Laboratory Technologist

Dr. S. K. T. P. Dayanath
Consultant Chemical Pathologist, NCTH

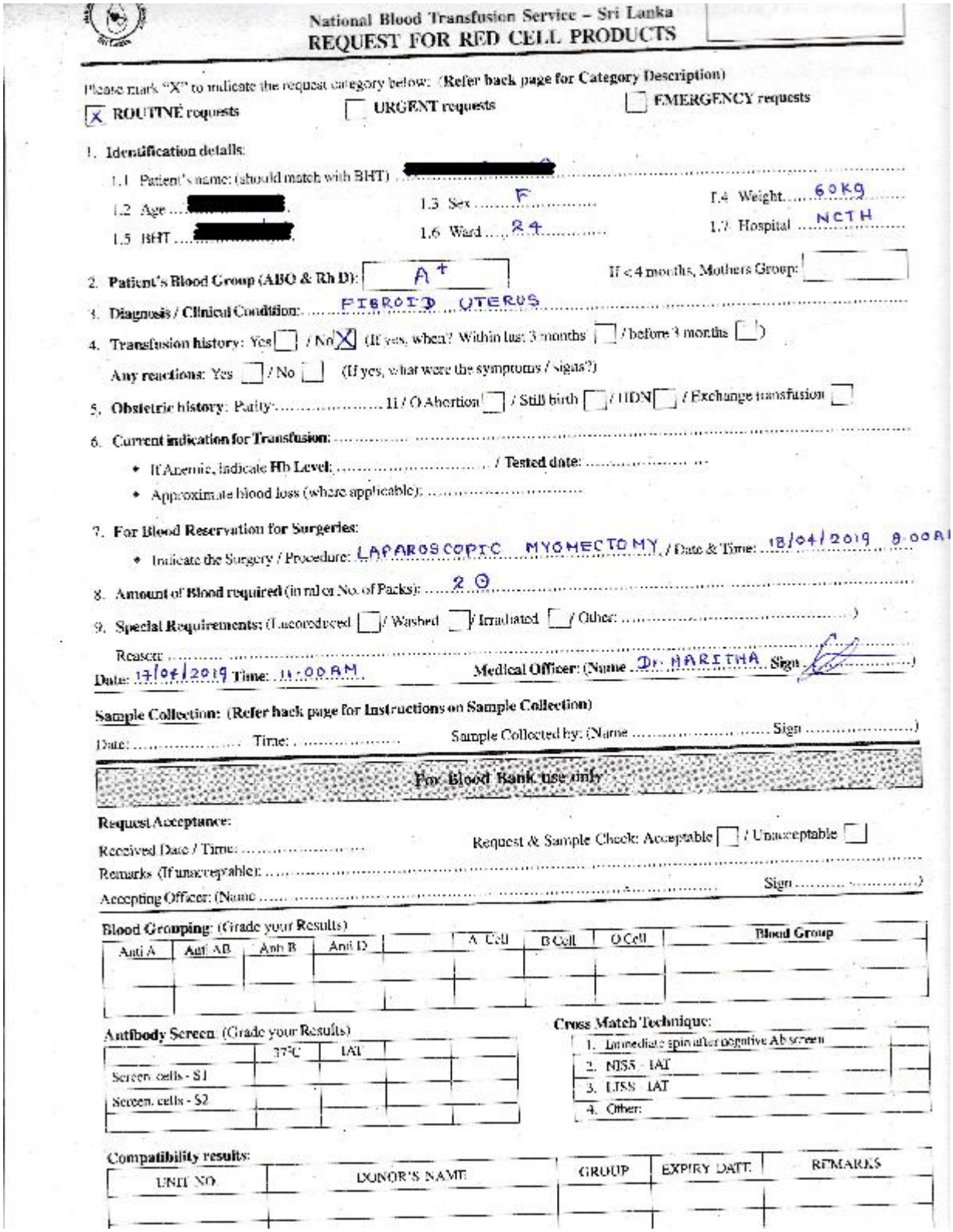
Date

EQAS
EXTERNAL QUALITY ASSURANCE SCHEME

Assay performed by Enhanced Chemiluminescence Immunoassay

Internal Quality Control : Vitros Immunodiagnostic control
External Quality Control : BIORAD EQAS USA

5.5 Request form for red cell products



National Blood Transfusion Service – Sri Lanka

REQUEST FOR RED CELL PRODUCTS

Please mark "X" to indicate the request category below: (Refer back page for Category Description)

[X] ROUTINE requests [ ] URGENT requests [ ] EMERGENCY requests

1. Identification details:
   - 1.1 Patient's name: (should match with BHT) [redacted]
   - 1.2 Age [redacted]
   - 1.3 Sex F
   - 1.4 Weight 60KG
   - 1.5 BHT [redacted]
   - 1.6 Ward 24
   - 1.7 Hospital NCTH
2. Patient's Blood Group (ABO & Rh D): A+ If < 4 months, Mothers Group:
3. Diagnosis / Clinical Condition: FIBROID UTERUS
4. Transfusion history: Yes [ ] / No [X] (If yes, when? Within last 3 months [ ] / before 3 months [ ])
   Any reactions: Yes [ ] / No [ ] (If yes, what were the symptoms / signs?)
5. Obstetric history: Parity: ..... 11 / 0 Abortion [ ] / Still birth [ ] / HDN [ ] / Exchange transfusion [ ]
6. Current indication for Transfusion: .....
   - If Anemic, indicate Hb Level: ..... / Tested date: .....
   - Approximate blood loss (where applicable): .....
7. For Blood Reservation for Surgeries:
   - Indicate the Surgery / Procedure: LAPAROSCOPIC MYOMECTOMY / Date & Time: 18/04/2019 8.00AM
8. Amount of Blood required (in ml or No. of Packs): 2 0
9. Special Requirements: (Leucoreduced [ ] / Washed [ ] / Irradiated [ ] / Other: .....)

   Reason: .....

Date: 17/04/2019 Time: 11:00AM Medical Officer: (Name Dr. HARITHA Sign .....)

Sample Collection: (Refer back page for Instructions on Sample Collection)

Date: ..... Time: ..... Sample Collected by: (Name ..... Sign .....)

For Blood Bank use only

Request Acceptance:

Received Date / Time: ..... Request & Sample Check: Acceptable [ ] / Unacceptable [ ]

Remarks (If unacceptable): .....

Accepting Officer: (Name ..... Sign .....)

Blood Grouping: (Grade your Results)

Anti A	Anti AB	Anti B	Anti D	A Cell	B Cell	O Cell	Blood Group

Antibody Screen: (Grade your Results)

	37°C	IAT
Screen. cells - S1		
Screen. cells - S2		

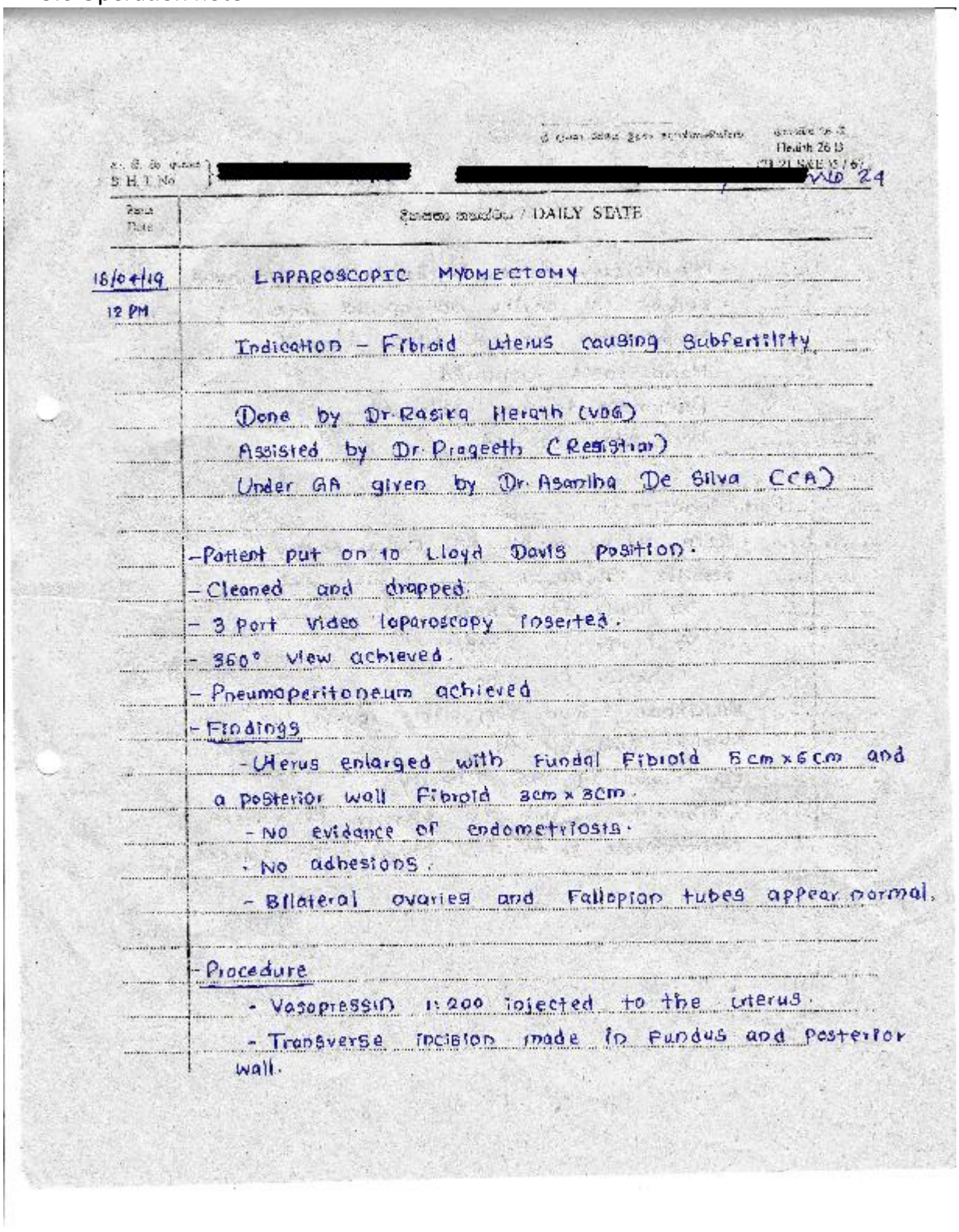
Cross Match Technique:

1. Immediate spin after negative Ab screen
2. NISS - IAT
3. LISS - IAT
4. Other:

Compatibility results:

UNIT NO	DONOR'S NAME	GROUP	EXPIRY DATE	REMARKS

5.6 Operation note



S.H.I. No [redacted] VVD 24

Date | DAILY STATE

16/04/19 12 PM

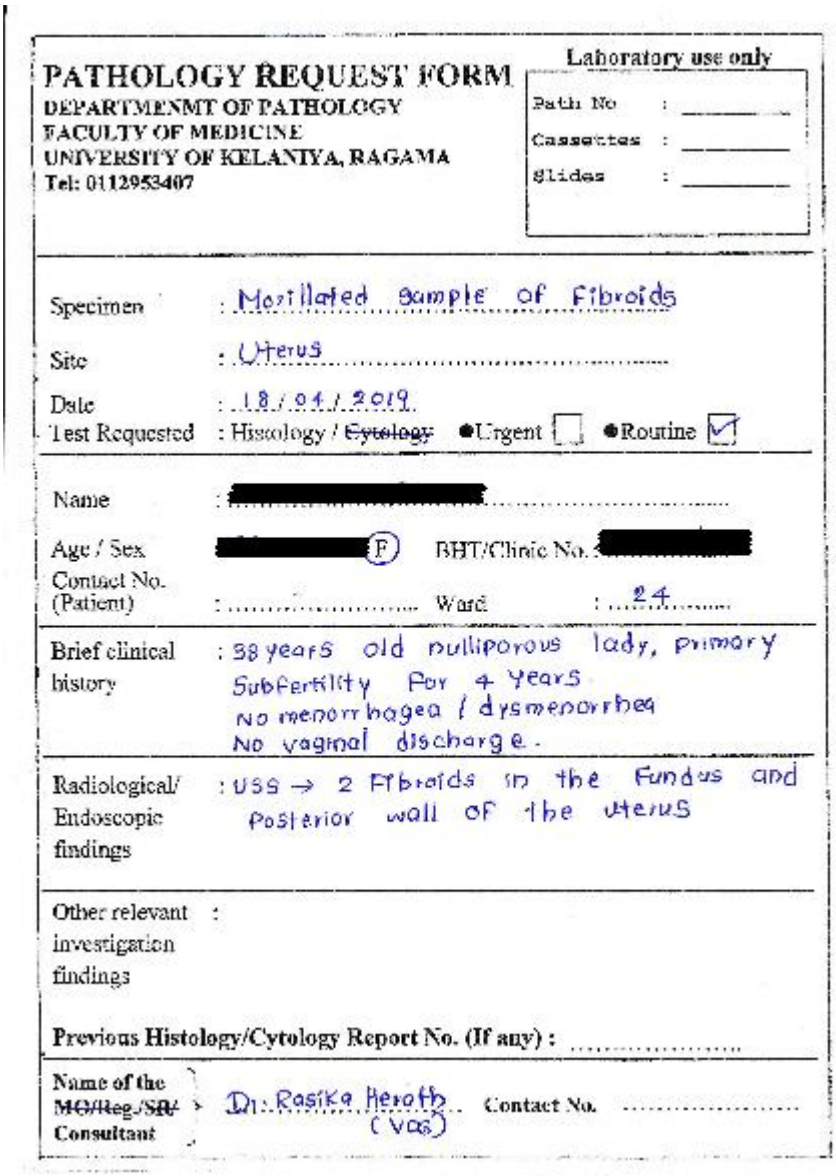
LAPAROSCOPIC MYOMECTOMY

Indication - Fibroid uterus causing subfertility

Done by Dr. Rasika Herath (VOG)
Assisted by Dr. Prageeth (Registrar)
Under GA given by Dr. Asanka De Silva (CCA)

- Patient put on to Lloyd Davis position.
- Cleaned and draped.
- 3 port video laparoscopy inserted.
- 360° view achieved.
- Pneumoperitoneum achieved
- Findings
  - Uterus enlarged with fundal Fibroid 5cm x 6cm and a posterior wall Fibroid 3cm x 3cm.
  - No evidance of endometriosis.
  - No adhesions.
  - Bilateral ovaries and Fallopian tubes appear normal.
- Procedure
  - Vasopressin 1:200 injected to the uterus.
  - Transverse incision made in Fundus and Posterior wall.

5.7 Pathology request form



PATHOLOGY REQUEST FORM

DEPARTMENMT OF PATHOLOGY
FACULTY OF MEDICINE
UNIVERSITY OF KELANIYA, RAGAMA
Tel: 0112953407

Laboratory use only

Path No : _____
Cassettes : _____
Slides : _____

Specimen : Mortilated sample of fibroids
Site : Uterus
Date : 18/04/2019
Test Requested : Histology / ~~Cytology~~ ●Urgent ☐ ●Routine ☑

Name : [redacted]
Age / Sex [redacted] (F) BHT/Clinic No. [redacted]
Contact No. (Patient) : ..... Ward : 24

Brief clinical history : 38 years old nulliporous lady, primary Subfertility for 4 years
No menorrhagea / dysmenorrhea
No vaginal discharge.

Radiological/ Endoscopic findings : USS → 2 Fibroids in the Fundus and Posterior wall of the uterus

Other relevant investigation findings :

Previous Histology/Cytology Report No. (If any) : .....

Name of the ~~MO/Reg./SR/~~ Consultant : Dr. Rasika Herath (Vas) Contact No. .....