Myomectomy versus abdominal hysterectomy in the management of uterine fibroid

By

Dr. Tasneem Mohammed Tag Elsir
M.B.B.S (University of Juba)

A thesis Submitted in partial fulfillment for the requirements of the degree of Clinical MD in Obstetrics and Gynecology

Supervisor

Pro.A/ Salam Gerais
FRCOG, MD
CONTENTS

Dedication .............................................................................................................I
Acknowledgment .................................................................................................II
Abbreviations .......................................................................................................III
English abstract .....................................................................................................IV
Arabic abstract ......................................................................................................V
List of figures .......................................................................................................VI
List of tables .........................................................................................................VII

CHAPTER ONE
INTRODUCTION AND LITERATURE REVIEW ...............................................1
OBJECTIVES .........................................................................................................36

CHAPTER TWO
PATIENTS & METHODS ....................................................................................37

CHAPTER THREE
RESULTS .............................................................................................................39

CHAPTER FOUR
DISCUSSION .........................................................................................................61
CONCLUSION .........................................................................................................66
RECOMMENDATIONS ..........................................................................................67
REFERENCES .........................................................................................................68
APPENDIX (Questionnaire)
To every woman who tolerated pain and performed
the miracle of bringing a new life to this world

And

To every doctor who tries earnestly to decrease the
sufferings of patients and make their lives easier and
happier
Acknowledgements

I would like to express my sincere thanks to Professor Abdel Salam Gerais, Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Khartoum, for his unlimited guidance, encouragement and very valuable advice in supervising this thesis. It was a privilege to be supervised by him.

I am greatly indebted to Doctor Mohamed Elias, Department of Obstetrics and Gynaecology, Omdurman Teaching Hospital, for originally suggesting the topic of this thesis. He helped me a lot in constructing the questionnaire. Without him this work would not have been realized.

I am also grateful to Doctor Mohamed Awad, Department of Obstetrics and Gynaecology, Soba University Hospital, for his invaluable assistance spending a great deal of his spare time in revising and analyzing this thesis.

My appreciation is extended to my family for their patience and diligence in typing and printing this thesis. Without their help I could never have completed the work.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>bFGF</td>
<td>Basic fibroblast growth factor</td>
</tr>
<tr>
<td>EGF</td>
<td>Epidermal growth factor</td>
</tr>
<tr>
<td>EBAF</td>
<td>Endometrial bleeding associated factor</td>
</tr>
<tr>
<td>GM-CSF</td>
<td>Granulocyte macrophage colony stimulating factor</td>
</tr>
<tr>
<td>GnRH</td>
<td>Gonadotropin_releasing hormone</td>
</tr>
<tr>
<td>Gyne.</td>
<td>Gynaecology</td>
</tr>
<tr>
<td>hGH</td>
<td>Human growth hormone</td>
</tr>
<tr>
<td>HMGIC</td>
<td>High mobility group protein IC</td>
</tr>
<tr>
<td>HPF</td>
<td>High power film</td>
</tr>
<tr>
<td>MCP 1</td>
<td>Monocyte chemotactic protein 1</td>
</tr>
<tr>
<td>MMP</td>
<td>Matrix metalloproteinase</td>
</tr>
<tr>
<td>mRNA</td>
<td>Messenger RNA</td>
</tr>
<tr>
<td>Nd:YAG</td>
<td>Neodymium:yttrium aluminum gamet</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Nonsteroidal anti-inflammatory Drugs</td>
</tr>
<tr>
<td>Obs.</td>
<td>Obstetric</td>
</tr>
<tr>
<td>OCPs</td>
<td>Oral contraceptive pills</td>
</tr>
<tr>
<td>TGF_beta</td>
<td>Transforming growth factor beta</td>
</tr>
</tbody>
</table>
Abstract

Fibroids are tumours of smooth muscle; usually they arise in the uterus where they may be very numerous. They are found in all races and any age after puberty.

This is a descriptive prospective hospital based study, carried out in three hospitals in Khartoum state in the period from the 15th of September 2004 to the 15th of March 2005 to find factors which affect the type of operation done for myoma treatment and to know its complications and outcome.

A total of one hundred and fourteen women were included in the study.

Information about personal data, parity, and present history of the patient, size, site and number of the fibroids in addition to the intraoperative and postoperative periods was collected using a questionnaire.

The type & timing of intervention in the treatment of fibroids should be individualized to each patient according to many factors including age and future fertility plans.

It was found that myomectomy was the commonest used modality of treatment used in 67.5% of population. The majority of women (75.5%) were between 30 to 45 years old and the majority of them were nulliparous.

Nearly half of the women (50.9%) were asymptomatic, while menstrual disorders occurred in 25.4% of the study population and pressure symptoms in 23.7%.

Women with fibroids of more than 16 weeks size were treated mostly with abdominal hysterectomy. Most of the women (61.4%) had more than one fibroid. The recurrence rate of fibroids was close to that in the literature.

Abdominal hysterectomy was associated with more intraoperative blood loss and more blood transfusion, while myomectomy was associated with more postoperative complications.

It was recommended that women should be counseled that hysterectomy is associated with less postoperative complication than myomectomy.
ملخص الأطروحة

الجرم في النمو والصحة العضلية في ورم مياء، أو مفردة تكون أنها يمكن متعددة، البالغة بعد الأعمار وكل في_matched_with. هذه الخرطوم محاكاة في مستشفيات ثلاثة في مسار معجلة وصفية دراسة المرأة، وهي منائر الاربعية لنع عن طريق. الاضطقاء والتفاوت والنتائج المضافات ومعرفة الأمراض. توافق الأمثلة، والمسيرة من المعلومات، والأماكن والحجم على جمعة بالمستشفى، والمرضى من الناحية، والمسيرة في الاتجاه. وراء الفقرة، والمسيرة، وبعدين الجهاز، والمسيرة في الاتجاه.

واقل من الأبواب، كفاءة البار، إذا كان في ثلاث سنة 2010، بالنسبة للمسيرة والمسيرة في الاتجاه.

اللذات مسير، propName. تفشي كفاءة البار، إذا كان في ثلاث سنة 2010، بالنسبة للمسيرة والمسيرة في الاتجاه.

الأسرة

(67.5%) نسبة، والنساء، كانت بين 30-40 سنة، بينما (25.4%) نسبة، و (&) نسبة، في الرجعية) 23.7

. يعود إلى

(2009) هنالك، بعض الأدلة، على أن الأنواع

. من بين

. من بين

. من بين

. من بين

. من بين

. من بين

. من بين

. من بين

. من بين

. من بين

. من بين

. من بين

.
## List of tables:

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Table 1</td>
<td>Type of operation and age</td>
<td>37</td>
</tr>
<tr>
<td>Table 2</td>
<td>Type of operation and marital status</td>
<td>38</td>
</tr>
<tr>
<td>Table 3</td>
<td>Type of operation and parity</td>
<td>39</td>
</tr>
<tr>
<td>Table 4</td>
<td>Type of operation and size of fibroid</td>
<td>40</td>
</tr>
<tr>
<td>Table 5</td>
<td>Type of operation and number of fibroids</td>
<td>41</td>
</tr>
<tr>
<td>Table 6</td>
<td>Type of operation and site of fibroids</td>
<td>42</td>
</tr>
<tr>
<td>Table 7</td>
<td>Site of fibroid and presenting symptoms</td>
<td>43</td>
</tr>
<tr>
<td>Table 8</td>
<td>Site of fibroid and infertility</td>
<td>44</td>
</tr>
<tr>
<td>Table 9</td>
<td>Type of operation and hemoglobin concentration</td>
<td>45</td>
</tr>
<tr>
<td>Table 10</td>
<td>Type of operation and need of blood transfusion</td>
<td>46</td>
</tr>
<tr>
<td>Table 11</td>
<td>Type of operation and duration of hospital stay</td>
<td>47</td>
</tr>
<tr>
<td>Table 12</td>
<td>Type of operation and postoperative complications</td>
<td>48</td>
</tr>
</tbody>
</table>
## List of figure

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Figure 1</td>
<td>Type of operation</td>
<td>49</td>
</tr>
<tr>
<td>Figure 2</td>
<td>Infertility</td>
<td>50</td>
</tr>
<tr>
<td>Figure 3</td>
<td>Duration of infertility</td>
<td>51</td>
</tr>
<tr>
<td>Figure 4</td>
<td>Presenting symptoms</td>
<td>52</td>
</tr>
<tr>
<td>Figure 5</td>
<td>Past obstetric and gynecological history</td>
<td>53</td>
</tr>
<tr>
<td>Figure 6</td>
<td>Type of anesthesia</td>
<td>54</td>
</tr>
</tbody>
</table>
CHAPTER
ONE
INTRODUCTION AND LITERATURE REVIEW

Fibroids are the commonest solid tumours of female genital tract and are found in all races and any age after puberty \(^{(1)}\), they are found in 20%–25% of women aged over 35 years and rarely grow after the menopause \(^{(2)}\).

Risk factors for clinically significant fibroids are nulliparity, obesity, a positive family history and African racial origin \(^{(3)}\).

A fibroid is a tumour of smooth muscle with a supporting structure of fibrous tissue. Some hyaline degeneration is present in all but smallest tumours and may be very extensive. Cystic degeneration in the centre of large fibroids is not uncommon; it is apparently due to avascular necrosis. Acute massive necrosis of fibroids occurs occasionally as a result of torsion or trauma. If the pedicle of a pedunculated subserous fibroid twists gradually, the omentum or sometimes the gut may adhere to the sticky fibrinous surface of the fibroid and eventually provide it with a blood supply which will keep it alive after its pedicle has sloughed. Red degeneration is almost always associated with pregnancy; its cause is unknown. Rarer, but of greater clinical significance is the marked cystic change occurring in large, usually subserous, fibroids during the later weeks of pregnancy \(^{(1)}\). Leiomyosarcoma develops from a myoma with a recorded incidence of 0.1–0.5% \(^{(4)}\).

Fibroids may be of any size from microscopic to massive \(^{(1)}\), weighing more than 45 kg (100 lb) \(^{(4)}\). Usually they arise in the uterus where they may be very numerous and are described according to their position as subserous, intramural or submucous. In Africa, the United States and the West Indies fibroids seem to be commoner to develop earlier and to grow larger in Negro women than in Europeans. This is probably a true racial difference. Fibroids are frequently associated with primary or secondary infertility \(^{(1)}\).

Pelvic inflammatory disease is frequently found in association with fibroids. \(^{(1)}\)

The term fibroid has the sanction of long usage and will probably continue to be applied to this benign smooth muscle tumour of the uterus, although the alternative terms myoma, fibromyoma and leiomyoma are more precise \(^{(1)}\).

Classification:
Uterine myomas originate in the myometrium and are classified by anatomic location. Submucous myomas lie just beneath the endometrium and tend to compress it as they grow toward the uterine lumen. They may develop pedicles and protrude fully into the cavity or even pass through the cervical canal while still attached within the corpus by along stalk. Here they are subject to torsion or infection.

Intramural or interstitial myomas lie within the uterine wall, giving it a variable consistency.

Subserous or subperitoneal tumors may lie just at the serosal surface of the uterus or may bulge outward from the myometrium. These external tumors tend to become pedunculated. If such a tumor acquires an extraterine blood supply from omental vessels, its pedicle may atrophy and resorb; the tumour is then said to be parasitic.

Aetiology:

The aetiology of fibroids is unknown; indeed, it is not certain whether they should be regarded as true tumors or as a form of hyperplasia of the myometrium. The cause of leiomyomas of the uterus is not known. Oestrogen stimulation of susceptible fibromuscular elements has been suggested. Myomas are known to increase in size with high dose oestrogen therapy and during pregnancy. Moreover, they decrease in size and even disappear following menopause. Nevertheless, there is no solid evidence to suggest that oestrogens cause leiomyomas.

The hypothesis that human growth hormone (hGH) is related to the development of myomas has been largely dispelled by radioimmunoassay studies of hGH in pregnant patients and in patients taking estrogens.

Epidemiology and risk factors:

Leiomyomas have not been described in prepubertal girls, but they are occasionally noted in their thirties or forties, being detectable clinically in about 20% of women over 30 years of age, and in approximately 80% of surgically removed uteri. Autopsy studies with systematic histology of the uterus show a prevalence of up to 50%.

Relief of symptoms related to fibroids usually occurs at the time of menopause, when menstrual cyclicity and steroid hormone levels wane. However, the increasing
prevalence of hormone replacement therapy in the post reproductive years has led to more reports of women who become symptomatic or continued to have symptoms after the menopause. (5, 6)

Other reproductive factors that affect the risk of developing a leiomyoma include:
- Parity (having one or more pregnancies extending beyond 20 weeks) decreases the chance of fibroid formation. (7–9).
- Oral contraceptive pills (OCPs) can protect against clinically evident fibroids. In data provided by the Nurses Health Study, OCPs use increased risk of leiomyomas with early exposure to OCPs between the ages of 13 & 16. (9).
- Smoking decreases the risk of having fibroids through an unknown mechanism. Smoking does not appear to affect estrogen metabolism. (7, 10)
- Significant consumption of beef, ham, or other red meats is associated with increased relative risk of fibroids and consumption of green vegetables with a decreased risk. (11).
- The relative risk of fibroids is two to three fold greater in black than in white women. (12) Among women undergoing hysterectomy, black women are significantly more likely to have leiomyomas, to be younger at the time of diagnosis of fibroids and at hysterectomy, and to have more severe disease (e.g. higher uterine weights, greater likelihood of anaemia). (13)
- Myomas are also common in obese women. (14)
- Other risk factor is positive family history. (3)

Although there are high levels of both estrogen and progesterone during pregnancy and with OCPs use, both decrease the risk of fibroids. Thus influences other than steroid hormones are important to fibroid growth. It is possible that myoma formation is a response to injury, much like an atherosclerotic plaque that forms in response to hypoxia of arterial muscle Hypoxia of myometrial cells during menstruation may promote transformation of normal myocytes to abnormal myocytes and subsequent leiomyomas. (15)

Pathology:
A fibroid is a benign tumor of uterine smooth muscles termed a leiomyoma. (3)

It is rare that only single myoma develops, they are usually multiple, discrete and spherical or irregular lobulated. (4)
On gross examination, in transverse section, the tumour is buff-colored, rounded, smooth and usually firm. Generally they are lighter in colour than the myometrium. There is no true capsule to myomas; however the progressing borders produce compression of the surrounding tissues and production of the so-called pseudocapsule. It is a thin layer of areolar tissue and compressed muscle fibres, through which the blood vessels enter the myoma. This pseudocapsule is useful in delineating the margin of the tumour during surgical resection and it allows for the easy shelling out of the myomas from their uterine bed.

On microscopic examination myomas display a proliferation of mature smooth muscle cells arranged in a trabeculated or whorled configuration. The muscle fibers are arranged in interlacing bundles. Fibrous connective tissue extends between the muscle bundles and is proportional to the amount of atrophy and degeneration. The myocytes are of spindle-shaped muscle cells, with elongated nuclei remarkably uniform in size, and the nuclear cytoplasm gives a characteristic benign appearance. At its periphery, the muscle fibres are arranged in concentric layers, and the normal muscle fibers surround the tumour are similarly oriented.

Myomas are originally located within the myometrium (intramural); however when noted clinically, they may be submucous, subserous, intraligamentous, pedunculated or parasitic.

Those tumours expanding toward the endometrial cavity and tend to compress the endometrium become submucous, or if further growth occurs, they may expand on a pedicle and eventually protrude from the cervical os becoming necrotic or infected.

Growth towards the peritoneal cavity produces the typical irregular contours noted clinically. It may be just at the serosal surface of the uterus, or they can have a broad or pedunculated base, bulge outward from the myometrium. It may be intraligamentary i.e extending between the folds of the broad ligament.

If the pedicle of a pedunculated sub-serous fibroid twists gradually, the ischemic/partially necrotic mass may then be isolated by the omentum or the bowel mesentery, re-establishing a blood supply and becoming so called parasitic leiomyoma.

The long term outcome of leiomyoma, like other tissues depends on the maintenance of vascular supply. As the entire blood supply of the myoma is derived from
one or two arteries entering from the pseudocapsule, the growth of the tumour means that it often outstrips its blood supply. This lead to degeneration, particularly in the central portion of the myoma: hyaline, cystic, calcific, fatty and red degeneration have been described (17).

**Hyaline degeneration:**

Is the most common and mildest form of degeneration, occurring in 60% of myomas. The smooth muscle cells are replaced by fibrous connective tissue. The cut surface no longer demonstrates the original whorled appearance. Histologically, the cellular detail is lost as replacement by fibrous tissues continues (16).

**Cystic degeneration:**

Occurs when hyaline changes continue to affect the myoma. These tumours may become liquefied and form cavities filled with clear or gelatinous material. The change may be so severe that the myoma becomes a hollow cavity and develops the appearance of a cystic mass. Cystic change occurs in approximately 2% of myomas (16).

**Fatty degeneration:**

Is rare and results from severe hyaline degeneration. The presence of true fat in a myoma is uncommon; however, the degenerated myoma may develop a yellowish fatty appearance (16).

**Calcific degeneration:**

Occurs in 4-10% leiomyomas when calcium carbonate and phosphate are deposited in areas of necrosis. The calcification may be diffuse, solid or circumferential. Thompson and Rock refer to these tumours as "womb stones" in their extensive treatise on the subject of leiomyomas. These are seen on x-ray film incidentally in postmenopausal women (16).

**Carneous or red degeneration:**

Occurs in rapidly growing myomas, e.g., during pregnancy. This may cause severe abdominal pain of a sudden onset and tenderness localised to an area of the uterus, associated with mild pyrexia and leucocytosis. The symptom and signs typically resolve over a few days and surgical intervention is rarely required. Degeneration is essentially an ischemic, necrotic degeneration caused by loss of blood supply, and the red color is
secondary to thrombosis and extravasation of blood into the myometrium giving it a raw beef appearance\textsuperscript{(16)}.

Infections may occur in any myoma, but they occur more commonly in those with advanced degeneration or relapse. Thompson and Rock quote one case of clostridium tetani in a myoma. In severe cases of intramural necrosis and infection, frank peritonitis and sepsis may develop. However, these cases are rare\textsuperscript{(16)}.

Rarely malignant/sarcomatous changes may occur\textsuperscript{(4)}.

Many histologic variations of myomas have been described: cellular, atypical, epitheliod, lipoleiomyomas and leiomyoma with tubules\textsuperscript{(18)}.

Cellular leiomyomas are composed of small cells with scanty cytoplasm and may be confused with leiomyosarcomas\textsuperscript{(16)}.

Atypical leiomyomas contain atypical cell clusters distributed throughout the tumour\textsuperscript{(16)}. There are uniform smooth muscle cells with a level of mitotic activity of between two and nine mitoses per ten high power field (HPF)\textsuperscript{(19)}. This variant is called a smooth muscle tumour of uncertain biological behaviour. Also called “bizarre” or “symplastic” and are also often confused with leiomyosarcomas\textsuperscript{(16)}.

The epitheliod variant is composed of plump eosinophilic tumour cells. However, even when epitheliod leiomyoma has only low mitotic activity (two to four per 10 HPF) metastasis may occur\textsuperscript{(19)}. It includes leiomyoblastoma, clear cell leiomyoma, and plexiform leiomyoma as described by Kuman and Norries\textsuperscript{(20)}. Coagulative necrosis (rather than hyaline necrosis or infraction) in fibroid is a sinister feature associated with recurrence and metastasis\textsuperscript{(19)}.

Myxoid change is an extension of hyaline change, with mucinous material visible macroscopically on the cut surface of the fibroid, and produces a myxoid leiomyoma. Extensive myxoid change results in cystic change. When cystic change occurs rapidly it can be painful. These tumours behave like epitheliod leiomyosarcoma and tend to be aggressive\textsuperscript{(19)}.

Leiomyosarcomas have large areas of fat and are diffuse or circumscribed. Leiomyomas with tubules have epithelium-lined tubules and are uncommon. Mesothelial differentiation also occurs\textsuperscript{(16)}.
Intravenous leomyomatosis is a very rare condition in which benign smooth muscle cells grow into veins. The principle symptoms and signs are of abnormal bleeding per vaginum and dull abdominal pain. Microscopically, tumour is seen in veins of diffuse sizes; arteries are not involved. All of the above subtypes of leiomyoma can for intravascular leomyomatosis, and the prognosis is same for all types. Treatment is by hysterectomy and bilateral salpingo-ophorectomy and unexpectedly the prognosis is good even when the lesion has not been completely excised. It may extend as rubbery cards beyond the uterus into the parametrium or occasionally into the vena cava. Some patients may survive for prolonged periods in spite of incomplete resection of the disease (21).

Leiomymatosis peritonealis dissaminata is a condition in which numerous nodules of histologically benign smooth muscle are present on peritoneal surfaces. It is frequently associated with a term pregnancy or with the use of oral contraceptives, and regression may occur after termination of the pregnancy (21).

**PATHOPHYSIOLOGY:**

The pathophysiology of leiomyomas is not well understood. A range of hypotheses according for the pathogenesis of fibroid has been explored.

The key features of uterine leiomyomata are their occurrence during reproductive years, where ovarian hormones levels are high, their diverse manifestations as either single or multiple tumours, and the existence of racial and familial predisposition (3). So genetic predisposition, steroid hormones, and growth factors are important factors in fibrotic processes and angiogenesis all play a role in the formation and growth of these tumors (22).

At least two distinct components contribute to leiomyoma development:

- Transformation of normal myocytes into abnormal myocytes.
- Growth of abnormal myocytes into clinically apparent tumours.

The first process appears to be quite common, in view of the high prevalence of microscopic myomas (23). The subsequent growth of the neoplasm occurs via clonal expansion from a single cell (24,25).
The possibility of abnormal oestrogen receptor expression has been explored and discounted; both main progesterone receptor subtypes are expressed similarly in myoma and normal myometrium. Thus myoma tissue is still influenced by ovarian hormones. Experimentally, progesterone has been shown to stimulate the production of both an apoptosis-inhibiting protein and epidermal growth factor (EGF) in cultured myoma tissue. Oestrodial has the effect of stimulating expression of EGF receptor

Growth factors:

Leiomyomas can be described as a fibrotic process manifested by up regulation of types 1 and 111 collagen, the major components of the extracellular matrix, that distinguish leiomyomas from the normal myometrium. The angiogenic growth factor basic fibroblast growth factor (bFGF) and its receptor appear significantly altered in the leiomyomatous uterus as illustrated by the following observations:

- There is more bFGF mRNA in leiomyomas than in normal myometrium.
- The extracellular matrix of myomas contains a large reservoir of bFGF.
- There is abnormal expression of the type 1 bFGF receptor in the myometrium of women with leiomyoma-related bleeding compared to normally cycling women.
- bFGF stimulates proliferation of leiomyoma cells in culture. This process is inhibited by interferon-alpha, a factor known to block the action of bFGF in other systems.

Transforming growth factor-beta (TGF-beta) and granulocyte-macrophage colony stimulating factor (GM-CSF) which are involved in other fibrotic processes, may also contribute to the pathophysiology of leiomyomas when obtained from the secretory phase of the menstrual cycle, leiomyomas appear to have higher levels of TGF-beta and TGF-beta receptor mRNA and protein than the myometrium. In addition, there is a substantial reduction in TGF-beta levels in the leiomyomas of women treated with a gonadotropin-releasing hormone GnRH-agonist to diminish the size of their tumors prior to surgical extirpation.

GM-CSF may differentially stimulate leiomyomas and normal myometrium both on its own and through an increase in expression of TGF-beta. A TGF-beta homologue, endometrial bleeding-associated factor (EBAF), which is normally expressed in the endometrium only in the luteal phase of the menstrual cycle, is expressed throughout the
cycle in women with abnormal uterine bleeding of various aetiologies, including leiomyomas (30).

Reduced expression of growth inhibitory factors such as monocyte chemotactic protein 1 (MCP-1) may play a part in the loss of inhibition required for fibroid growth. Treatment by ovarian suppression is associated with an increase in matrix metalloproteinase (MMP) expression and a decrease in metalloproteinase inhibitory activity, which suggest that ovarian hormones have a role in maintaining the architecture of a myoma once formed (3).

GENETICS

Leiomyomas may be viewed as a common phenotype resulting from a number of different genetic events. There are a variety of specific karyotypic subgroups that characterize myomas; however, the evolution of a cytogenetic abnormality appears to be a late event (25).

Cytogenetic studies have identified specific features of uterine myoma tissue compared to normal myometrium and to leiomyosarcoma. It appears that cells within an individual myoma are monoclonal in origin, but cells from different myomas within the same uterus are of independent origin. It is likely that the clonal expansion of tumour cells precedes the development of cytogenetic aberrations, but the latter may determine the clinical course depending on the extent to which control over growth is lost. Some evidence for this is provided by cytogenetic analysis, which showed a greater proportion of karyotypic abnormality in larger, compared to smaller fibroids. The most common cytogenic aberrations have been detected on chromosome 12, 6, 3 and 7, a ring chromosome 1, and translocation involving chromosomes 12 and 14. Relevant areas of chromosomes 12, 6 and 7 are thought to contain putative growth-regulating or tumour-suppressor genes (3).

One gene, high mobility group protein 1 C (HMG 1C), appears to be dysregulated in the subgroup of myomas characterized by acquired 12 q 14-15 rearrangements. Myomas with this abnormality tend to be larger than those with a normal karyotype (31).

It is not yet clear to what extent the cytogenetic features can be correlated with the clinical picture (3).
Twin studies and family studies imply a familial predisposition to leiomyomas\textsuperscript{(32)}. As example in Reed’s syndrome uterine fibroids are found in kindreds with subcutaneous leiomyomas, and in Bannayan-Zonana syndrome they occur with other benign mesenchymal tumours (e.g. lipomas, hemangiomas)\textsuperscript{(33,35)}.

The possibility of malignant transformation of a fibroid to a leiomyosarcoma has traditionally been cited as a reason to recommend surgery for fibroids, with a stated risk of up to 0.5%. However, current opinion is that where a sarcoma develops in the presence of fibroids the association is coincidental, and that malignant transformation of a fibroid is unlikely. The cytogenetic evidence gives some basis for reassurance on this point as the typical findings in leiomyosarcoma tissue are of more extensive genetic instability, with frequent deletions especially involving chromosomes 1 and 10\textsuperscript{(3)}.

Vascular abnormalities:

Abnormalities in uterine blood vessels and angiogenetic growth factors also appear to play a role in pathology of myoma formation. The myomatous uterus has increased numbers of arterioles and venules, as well as venular ectasia (i.e. dilation)\textsuperscript{(36)}. Molecular alterations leading to increased vessel number or abnormal function are the likely mechanisms for the abnormalities, although the venous changes were originally thought to be induced by physical compression of the vascular structures by bulky myomas\textsuperscript{(25)}.

Clinical manifestations:

Most small myomata, and some larger ones, are symptomless and are only detected during a routine examination\textsuperscript{(17)}. It may be identified coincidentally, for example at the time of taking a cervical smear or performing laparoscopic sterilization\textsuperscript{(3)}.

The estimates of symptoms caused by uterine leiomyomas range from 10 to 40%. It is likely that the lower estimates more accurately reflect the incidence of symptoms due to the large number of known small asymptomatic myomas\textsuperscript{(16)}.

Symptoms from myomas depend upon their location, size, and state of preservation and whether or not the patient is pregnant\textsuperscript{(4)}.

Increased uterine bleeding:

The most common symptom associated with leiomyoma is abnormal uterine bleeding, most oftenly menorrhagia defined as > 80cc blood loss over the course of a menstrual flow. Interestingly >50% of women reporting blood loss have measured blood
loss that is within normal limits. Indeed, many women with even larger myomas may have regular menses of measurable duration and flow. Heavy bleeding does occur in approximately 30% of women with symptomatic bleeding presenting as both menorrhagia and metrorrhagia (16).

Abnormal bleeding is commonly thought to be associated with submucous or pedunculated myomas on the basis of either ulceration or necrosis. However, ulceration is rarely observed in hysterectomy specimens or at hysterectomy. Indeed, a study by Rubin and Ford indicates that the incidence of submucous myomas (5%) is too low to explain the incidence of menorrhagia (37). Sehgal and Haskins indicate that the surface area of the endometrial cavity may increase greater than 10 times with large myomas (38). As noted previously, the areas involved with myomas may have increased estrogen receptors and be relatively hyperestrogenic, leading to over-lying endometrial hyperplasia. Also Farrer-Brown et al, have noted alteration in vasculature in the areas of leiomyomas that may alter normal haemostatic mechanisms (39). Thompson and Rock recommend endometrial sampling even for patients who have regular menstrual flow (40).

Blood loss occurring over a long period of time may result in anaemia, weakness, dyspnoea and even congestive heart failure which must be treated before surgery (1).

Pelvic pressure and pain:

Myomas can occur as single or multiple tumors and range in size from microscopic to tens of centimetres. The size of the myomatous uterus is described in menstrual weeks, as with gravid uterus. A 20-weeks size myomatous uterus is not unusual; it is often associated with increasing girth and a sense of fullness similar to pregnancy (1).

Pelvic pain is a common reason cited for either myomectomy or hysterectomy; however myomas probably do not cause pain except in a few specific cases. Carneous degeneration or torsion, both of which may be caused by vascular ischemia, may cause pain or low grade fever, uterine tenderness on palpation, elevated white blood cells count, or peritoneal signs (16). The discomfort resulting from degenerated fibroids is self limited, lasting from days to a few weeks, and usually responds to nonsteroidal anti-inflammatory drugs. If acute pain is the sole indication for surgery, other disease processes, such as endometriosis and renal colic, should be carefully excluded (41).
Quite often the development of discomfort comes on insidiously and the symptoms are difficult for a patient to define. She may complain of pelvic pressure, congestion, bloating or a feeling of heaviness in the lower abdomen\(^{(41)}\).

Tumors that become impacted within the bony pelvis may press on nerves and create pain radiating to the back or lower extremities. Backache is such a common general complaint that it is usually difficult to ascribe it specifically to myoma\(^{(4)}\).

Pressure and obstructive symptoms may be reported in up to 30% of patients with uterine myoma. For example, uterine leiomyomas have purportedly caused urinary incontinence, and bulky myomas may cause frequency secondary to lack of adequate space for urinary bladder expansion. It is possible for an anterior myoma to impinge on the urinary bladder or the lower uterine segment or a cervical myoma to obstruct the urethra. Posterior myomas may press against the sigmoid, causing dyschezia and constipation\(^{(16)}\). According to an (ACOG) American College of Obstetrics and Gynecology technical bulletin, complete urethral obstruction has not been reported, but we and others have observed significant hydronephrosis in the presence of massive leiomyomas placing pressure on the pelvic brim\(^{(42)}\). Thompson and Rock report that this hydronephrosis is generally reversible if no parenchymal damage has occurred\(^{(40)}\). No studies appear to be available regarding degree of obstruction and alteration in renal function of patients with large, obstructing myomas or reversibility of the pathology if the obstruction is removed\(^{(16)}\).

Dyspareunia from cervical myomas proximate to the vagina is also common. It may be due to shortening and distortion of the vagina by fibroids low in the pelvis, or to adherent prolapsed tubes and ovaries in the pouch of Douglas, or to tender uterosacral ligaments associated with chronic cervicitis\(^{(1)}\).

There is a substantially increased incidence of secondary dysmenorrhea in women with uterine myomas\(^{(43)}\).

Rapidly enlarging uterine neoplasms are often attributed to leiomyosarcomas, although most women with this finding do not have a sarcoma. This was illustrated in a study of 1332 women admitted to two community hospitals for hysterectomy for presumed uterine leiomyomas, the incidence of uterine sarcomas was extremely low (0.23 %)\(^{(44)}\).
Among 321 women with a rapidly growing uterus by clinical or ultrasound examination, only one (0.27 %) had a sarcoma. Based upon these data, an increased risk of sarcoma among women with “rapidly growing” leiomyomas could not be substantial. However the diagnosis of a uterine sarcoma should be considered in postmenopausal women with a pelvic mass, abnormal bleeding, and pelvic pain in whom the incidence of sarcoma is higher (1 to 2 %) (45).

Effects on reproduction:

The risk of infertility is increased when the endometrial cavity is distorted by submucous leiomyomas (46). It may result from mechanical obstruction or occlusion of the fallopian tubes and it may prevent implantation of a fertile ovum (3).

By comparison, the role of intramural leiomyomas in infertility is controversial; some studies suggest myomas are sources of infertility (47); while more recent reports from women undergoing in vitro fertilization suggest they play a role (48,50). One case control study compared 106 women who had laparoscopic removal of their myomas to 106 women with unexplained infertility and no myomas. The delivery rate was highest among the group treated with myomectomy 42, 12 and 25 %, respectively (51).

Leiomyomas do not interfere with ovulation, but have been associated with infertility and adverse pregnancy outcomes in some (52,54) but not all (55,56) reviews.

Buttram and Rieter reported only 2-4 % of myomectomies were performed for myomas in the absence of other factors for infertility, they reported a significant reduction in spontaneous abortions (41% vs. 19 %) after myomectomy (57). The obvious possibility for causation of spontaneous, recurrent abortion may be present in the leiomyomatous uterus including endometrial obstruction, sub mucous myomas causing interference with implantation, placentation, and so forth. In addition, myomas have been associated with prematurity and still birth but no causal effects have been noted (16).

A population-based study of 2065 women with hospital discharge records indicating the presence of fibroids reported pregnancy outcomes based on birth certificate data (53). Compared to controls, women with fibroids were more likely to have abruption
placentae (OR 3.87), first trimester bleeding (OR 1.82), dysfunctional labour (OR 1.85), breech presentation (OR 3.98), and caesarean section (OR 6.39)\(^{(53)}\).

Approximately one third of women experience fibroid growth in the first trimester; the remaining women have stable or reduced tumour size during pregnancy\(^{(58, 59)}\). The risk of abruption appears to be related to the size and location of the myoma; it is substantially increased if the myoma is large (e.g. \(>\)or \(=\)6cm) or subjacent to the placental site \(^{(52, 53)}\). Other pregnancy complications noted in largely observational literature include pain, premature labour, retained placenta, and premature rupture of membranes \(^{(54, 60)}\).

After delivery, postpartum haemorrhage may occur due to inefficient uterine contractions \(^{(3)}\).

Other less common complications of fibroid include:
- Prolapse into the vagina resulting in ulceration or infection\(^{(61)}\).
- Polycythemia from autonomous production of erythropoietin\(^{(61)}\).

Uterine myomas may undergo torsion, infarction and/or necrosis during pregnancy, causing the patient to present with acute abdominal pain. The outcome of these occurrences is usually favourable with conservative management. However, if surgical management is directed by continued pain, infection, or other factors, several authors have reported satisfactory outcomes without excessive pregnancy loss. Other pregnancy complications include placental entrapment, lower-uterine segment or pelvic obstruction\(^{(16)}\).

Physical examination may establish the diagnosis in \(>\)90% of cases. The finding of enlarged, mobile, firm, irregular mass continuous with the cervix, on bimanual examination is almost always diagnostic\(^{(16)}\).

**Differential Diagnosis:** Other causes of an abdominopelvic mass in a woman in the reproductive years need to be considered \(^{(3)}\).

The uterus enlarged with fibroid is typically firm in contrast to that of a uterus enlarged with pregnancy\(^{(3)}\).

An ovarian tumour, whether benign or malignant, primary or secondary, may enlarge to occupy the pelvis and be difficult clinically to differentiate from a uterine fibroid \(^{(3)}\).
Leiomyosarcomas typically present with a history of a rapidly enlarging abdominopelvic mass. There may be less mobility of the uterus than expected with a fibroid and general signs of cachexia.

**Investigations:**

Imaging techniques are useful when it is necessary to confirm the diagnosis or to improve localization of the myoma prior to surgery; routine radiologic assessment is not required and does not improve outcome [American College of Obstetricians and Gynaecologists]. The various imaging modalities have the following advantages and disadvantages (Cohen).

- **Transvaginal ultrasound** has high sensitivity (95 to 100 percent) for detecting myomas in uteri less than 10 weeks' size. Localization of fibroids in larger uteri or when there are many tumors is limited.

- **Sonohysterography** improves characterization of the extent of invasion into the endometrial cavity by submucous myomas.

- **Hysterosalpingography** is a good technique for defining the contour of the uterine cavity. It has poor ability to visualize the rest of the myometrium and can falsely identify an intramural fibroid impinging on the uterine cavity as a submucosal fibroid.

- **Magnetic resonance imaging** is the best modality for visualizing the size and location of all uterine myomas and can distinguish among leiomyomas, adenomyosis, and adenomyomas. It may also be useful in differentiating leiomyomas from leiomyosarcomas.

- **Radiology with plain pelvic radiograph** may show the characteristic stippling of calcification in uterine fibroids. A soft tissue shadow can be visible in other films (such as excretion urography) and show indentations and pressure effects.

**Invasive diagnostic procedures:**

Diagnostic laparoscopy may be the only way to resolve a differential diagnosis between adnexal pathology and small eccentric fibroids that may not warrant therapy.

Hysteroscopy is particularly important in the diagnosis of intracavitary projection of benign uterine tumors, whether of the myometrium or endometrium. This procedure may often be carried out at a one-stop diagnostic outpatient clinic.
Laparotomy may be the only way that distinction between uterine leiomyomas and adenomyomas can be made, and permits histological confirmation (19).

**Treatment of uterine leiomyomas**

Both medical & surgical therapies are utilized in treatment of fibroids. Asymptomatic uterine leiomyomas are usually treated expectantly (62).

Factors that should be considered prior to initiating treatment include:
- size of the myoma(S)
- location of the myoma(s)
- symptoms
- woman's age (e.g., is she near menopause)
- reproductive plans

The type & timing of intervention should be individualized based upon the woman's discomfort, pregnancy plans & obstetrical history, and the likelihood of age or hormonal therapy-related progression of the neoplasms (63).

**Medical therapy:**

Benign tumors of the uterus, like the normal myometrium and endometrium from which they are derived, have oestrogen and progesterone receptors and are therefore open to attempts at hormonal manipulation (19).

**Gonadotropin-releasing hormone analogs:**

Gonadotropin-releasing hormone (GnRH) analogs are the mainstay of medical therapy of uterine myomas. These drugs work by initially increasing the release of goadotropins, followed by desensitization and down regulation to a hypogonadotropic, hypogonadal state clinically resembling menopause. Most women will develop amenorrhea and a significant reduction in uterine size with this therapy (64, 65). However, there is rapid resumption of menses and pretreatment uterine volume after discontinuation of the medication. In addition, significant symptoms can result from these severe hypoestrogenism that accompanies administration of GnRH-analogs (64). Bone loss leading to osteoporosis after long-term use is the most serious complication. For these reasons, GnRH-analogs are primarily employed to temporize or to help
prepare a woman for surgery. As an example, a meta-analysis of 19 randomized controlled trials found that GnRH analogs administered for three to four months prior to fibroid surgery reduced both uterine volume and fibroid size, helped to correct preoperative iron deficiency anemia, and lowered intraoperative blood loss. Preoperatively administered GnRH – analogs decrease blood loss at the time of surgery and increase the preoperative hematocrit when taken for two to three months before the procedure. Since oral iron supplementation alone will improve the preoperative hematocrit in significant number of patients, the cost and adverse effects of of GnRH agonists must be weighed against their efficacy. GnRH agonist therapy may not be cost effective in all women. In addition, this treatment may induce fibrous changes within the myoma capsule, thus making the lieomyoma difficult to remove. The drug has not been shown to increase the subsequent pregnancy rate or decrease adhesion formation. It is unclear whether the smaller uterine size that results from preoperative treatment allows more women to undergo myomectomy rather than hysterectomy.

The issue of GnRH agonists used preoperatively prior to hysterectomy has been investigated by several authors with relation to conversion from abdominal hysterectomy to vaginal hysterectomy, conversion from mid line to Pfannenstiel incision, and therapy for preoperative anaemia and operative complications.

**Recurrence after GnRH treatment:**

Lieomyomas can occur after myomectomy. one randomized study found no difference in the rate of recurrent fibroids developing over 27 to 38 months in women treated with a GnRH agonist compared to those treated with progesterone before surgery. Women who had at least four myomas removed were at greater risk of recurrence. However, other investigators have found an increased incidence of recurrent fibroids following GnRH agonist pretreatment (63 versus 13 percent).
Other:
Autologous blood donation may be indicated if intraoperative blood loss is likely greater than 500–1000 ml. In one series, twenty percent of women undergoing abdominal myomectomy required blood transfusion and 70% of these received autologous blood (73).

GnRH analogs with add back therapy:
The side effects of long term GnRH_analog administration can be minimized by giving add back therapy with an estrogen-progestin after the initial phase of down regulation. Low dose estrogen progestin therapy (equivalent to 0.625 mg of conjugated estrogen) maintains amenorrhea and the reduction in uterine volume while preventing significant hypoestrogenic side effects (e.g. osteoporosis, vasomotor symptoms) (74). Similar clinical results have been achieved with GnRH_ analogs. The advantage of these medications is the rapid onset of clinical effects and absence of an agonist phase. The antiprogestin mifepristone (RU_486) reduces uterine volume comparable to that observed with GnRH_agonists, but maintains the estradiol concentration in the early follicular range (75).

Danasol and gestrinone:
Danasol is a 19_nortestosterone derivative with progestin like effects. Its mechanism of action includes inhibition of pituitary gonadotropin secretion, direct inhibition of endometriotic implant growth, and direct inhibition of ovarian enzymes responsible for estrogen production. Since it induces amenorrhea, Danazol may control anemia due to fibroid related menorrhagia. A second androgenic steroid, gestrinone, decreases myoma volume and induces amenorrhea in women with fibroids. An advantage of this drug is that there is a carry-over effect after it is discontinued. In one study, for example, uterine volume remained lower than pretreatment values at 18
months after discontinuation of therapy in 89% of women treated for six months \(^{(76)}\).

**Ineffective therapies:**

Medical treatments that are commonly prescribed but appear ineffective include progestational agents and nonsteroidal anti-inflammatory drugs \(^{64, 77}\). However, they may be useful in women with coexisting problems. (e.g. Pain). \(^{(64, 77)}\)

**Progestational agents:**

Many algoryms for the treatment of abnormal bleeding due to myomas suggest a trial of oral contraceptives pills (OCPs) or progestin therapy prior to proceeding to definitive therapy. There is no evidence to suggest that these are effective therapies for myomas \(^{(64, 65)}\). However, oligoovulation and endometrial atrophy induced by hormonal therapy may help to decrease overall bleeding.

**Nonsteroidal anti-inflammatory drugs:**

Non steroidal anti-inflammatory drugs (NSAIDs) and anti fibrinolytic agents, which are useful in the treatment of idiopathic menorrhagia, have not been extensively studied in leiomyoma related menorrhagia. NSAIDs do not appear to reduce blood loss in women with myomas \(^{(77, 78)}\).

**Operative procedures:**

Surgery is the mainstay of therapy for leiomyomas. Hysterectomy is the definitive procedure, myomectomy by various techniques, endometrial ablation, and myolysis are alternative.

The surgical approach to myomectomy is dependent upon the location of the myomas. Myomectomy can be performed by laprotomy, transvaginally, laproscopically, or hysteroscopically. The abdominal approach is the gold
standard for women with intramural tumors, vaginal myomectomy is the most appropriate technique for prolapsed myomas, and hysteroscopic resection is the best choice for sub mucosal fibroids (79).

**Abdominal myomectomy:**

Myomectomy (resection of a myoma(s)) is an option for women who desire future pregnancies or otherwise wish to retain their uterus or improve pregnancy outcome after repetitive miscarriages. Abdominal myomectomy can be performed through a transverse or midline incision. Surgical principles are similar to those used for other gynecologic surgical and infertility procedures, meticulous hemostasis and avoidance of adhesiogenic materials (79).

A transabdominal myomectomy is the treatment of choice when there are multiple myomas or the uterus is significantly enlarged. The operative time, blood loss, and hospital stay are comparable to abdominal hysterectomy (79-80). The risk of unplanned hysterectomy at the time of myomectomy is less than 1% for the experienced surgeons (62).

**Hemostasis:**

Blood loss during myomectomy correlates with preoperative uterine size, total weight of fibroids removed, and operating time (81). Myometrial injection of vasoconstrictors such as vasopressin (made by diluting 10 to 20 U in 40 to 50 ml normal saline) help to control hemostasis. In a randomized placebo controlled trial, the use of vasopressin significantly reduced operative blood loss (225 versus 675 ml) (82). Other techniques include using a tourniquet (e.g. Penrose drain or catheter) (83), or a long vascular-type clamp with rubbershods applied over the clamp's jaws (84), to compress the uterine vasculature and infundibulopelvic ligaments.
Pharmacologic vasoconstriction and mechanical vascular occlusion are similarly effective (81). Employing electro surgery or laser for making the uterine incisions(s) also help to minimize blood loss (85-89).

**Reduction of adhesion formation:**

A posterior uterine incision should be avoided, if possible, because it is more likely to lead to postoperative adhesions. Copious irrigation with heparinized Ringer's lactate solution and moistened laprotomy packs may help to limit adhesion formation, placing these packs inside plastic packs reduces lint deposition. Adhesion prevention solutions (90) or application of adhesive barriers (e.g. Interceed, Gore-Tex) may be considered, but improvement in pregnancy rate is not certain (91).

**Uterine incision and myomectomy:**

The initial uterine incision should be large enough to allow removal of the maximum number of the number of incisions required. A vertical incision on the anterior uterine surface avoids the most vascular areas of the uterus. The incision is carried down to incise the myoma itself, this allows for identification of the plane between the myoma capsule and the myometrium. An Allis clamp or towel clip is placed on the myoma and traction is applied to help develop a plane between the myoma capsule and the myometrium using blunt and sharp dissection. Any loose connective tissue or vascular tissue between the capsule and myometrium is identified and the remaining connective tissue and blood supply are clamped and ligated. Electro surgery is used to desiccate any bleeding vessels. Every effort should be made to identify and remove all of the myomas (92). Most myomas can be identified by preoperative ultrasound.
and intraoperative visualization and palpation. Entry into the endometrial cavity should be avoided as this could lead to adhesion formation (e.g. ASherman's syndrome) or possibly result in uterine rupture with future pregnancy. Special care must be taken to avoid injury to the fallopian tubes during removal of cornual myomas.

The myometrial defect is closed with several layers of interrupted sutures of delayed absorbable material or a continuous suture in concentric circles. The serosa is reapproximated using a baseball type or subserosal suture (93).

**Outcome:**

A review of abdominal myomectomy in 128 women reported an average intraoperative blood loss of 342 ml, with five patients sustaining blood loss greater than 1,000 ml (73). Hysterectomy was required in only one woman. Febrile morbidity occurred in 12 women.

Although myomectomy is an effective therapy for menorrhagia and pelvic pressure, the disadvantages of this procedure is the significant risk that more leiomyomas will develop from new clones of abnormal myocytes. Five years after myomectomy, approximately 50% of patients will have myomas detected by ultrasound (94) and 11 to 26% will require a second surgery after the first myomectomy (95-97). The risk of uterine rupture after myomectomy prior to labor is very low (about 0.002%) compared to classical cesarean section, although these data are based upon a small series without complete pregnancy follow up. The common clinical practice of counseling women who have had a myomectomy with a transmural uterine incision to undergo an elective cesarean section clearly biases the reported risk of rupture at term. It is important to judge new surgical alternatives to abdominal
myomectomy according to their safety for women whose aim is future pregnancy (98-99).

**Vaginal myomectomy:**
Prophylactic antibiotics are generally recommended although data from randomized studies are not available. The pedicle of a prolapsed fibroid can be clamped across the base, cut, and sutured ligated using a delayed absorbable suture material. This is not always possible with large myomas; these tumors must be morcellated until the base can be identified. Alternatively, a pretied surgical loop may be passed over the myoma and the base ligated. A Foley catheter placed into endometrial cavity and inflated can be used to tamponade excessive bleeding. Sub mucous myomas that are not prolapsed require cervical dilatation (e.g. with laminaria tents or cervical dilators). The myomas are then removed by grasping them with uterine polyp forceps or uterine dressing forceps. A diagnostic hysteroscopy should be performed after removal to determine whether other submucous myomas are present. Hysteroscopic resection of additional tumors can be performed if the patient is stable (100).

**Outcome:**
The procedure is successful in greater than 90% of cases (101). Morbidity following vaginal myomectomy is lower than with the abdominal approach. A second vaginal myomectomy becomes necessary in approximately 9% of women over a five year follow up period; approximately 6% require hysterectomy (102).

**Laparoscopic myomectomy:**
Women with a uterus less than 17 weeks size or with a small number of subserosal or intramural fibroids can consider the option of laparoscopic
myomectomy (LM). The uterus must be small enough to allow visualization of the procedure through an endoscope placed at the umbilicus. Most authorities suggest limiting this procedure to the removal of three or fewer myomas and myomas not larger than 13 cm in diameter because this technique can take longer than open myomectomy, especially when laparoscopic suturing is employed. An electronic morcellator permits efficient removal of a large myoma in pieces through a small incision. Pretreatment with GnRH agonists reduced blood loss and operating time in some (103) but not all studies (70).

**Outcome:**

Several prospective randomized trials reported that the early outcomes of laparoscopic and abdominal myomectomy are similar. Laparoscopic procedures, however, are associated with less postoperative pain and a shorter recovery time (104). Whether reapproximation of the myometrium via laparoscopic suturing gives the uterine wall the same strength as multilayer closure at laparotomy is an area of controversy (105). The authors of case reports describing uterine rupture after LM as early as 33 or 34 weeks of gestation have suggested that women with intramural fibroids undergo laparotomy or modified laparoscopic closure. By comparison, one series of 100 deliveries after LM reported three cases of spontaneous uterine rupture, only one of which occurred in the LM scar. No uterine rupture occurred among the 72 patients who had a trial of labor. Until further data are available, laparoscopic myomectomy, especially when there is a deep intramural fibroid, should be used with caution in women whose primary goal is to achieve a pregnancy (106-107).

**Laparoscopic myolysis:**
A neodymium: yttrium aluminum gamet (Nd: YAG) laser can be used to coagulate and devascularise myomas through the laparoscope. This method involves pretreatment of women with a GnRH agonist for two to six months. Ten percent vasopressin solution is injected directly into the serosa of myomas. The Nd: YAG laser is set at 50 watts of power using 600 mm fiber. The bare fiber is used to pierce the myoma in multiple places at 5 mm intervals, thus, 75 to 100 puncture are used for a myoma measuring 5 cm. Myomas regress by 50-90% of their original volume over the three to six months following the procedure. Recurrences are infrequent, however, dense and fibrous adhesions can occur, thus, until additional data are collected; this procedure is only recommended for women who do not desire further child, but bearing who want to retain their uterus (108–109).

**Hysteroscopic resection:**

The ideal myoma for hysteroscopic removal is a pedunculated submucous myoma. A continuous flow hysteroscope allows optimal visualization because any bleeding can be easily cleared. The uterine cavity is distended with either a high-viscosity (e.g., Hyskon) or a low viscosity (e.g., 4% sorbitol) fluid media infused by gravity, although an electronic pump can be used. The tumor is gradually removed by applying a "shaving" technique through the resectoscope. Laparoscopy is performed routinely by some authors and must be done if there is any significant degree of intramural extension (109–110).

The submucous location of these tumors offers ready access to an operative endoscope placed through the cervix. Although this technique requires highly skilled practitioners, it has several advantages compared to abdominal procedures:
- It is performed as same day surgery.
- Local anaesthetic and sedation can be use
- The recuperation period is short.
- Good relief of symptoms is obtained. In one large series, fewer than 16% of women treated for menorrhagia underwent a second surgery in the nine year follow-up period \(^{(111)}\).

Fertility rates are excellent and there have been no case reports of uterine rupture after hysteroscopic myomectomy \(^{(112)}\).

**Pedunculated leiomyomas:**

Pedunculated myomas are cut near the pedicle base by positioning a wire loop behind the myoma and cutting the stalk with an electrosurgical (or laser) energy source. A pure cutting current is used to avoid having tissue stick on the loop itself. Special care should be taken to avoid disturbing the endometrium and surrounding myometrium.

The myoma is removed intact or after morcellation using a polyp forceps. Portions of the fibroid that can not be removed may be left inside the uterus and will undergo degeneration over a two to three week period \(^{(113)}\).

**Sessile leiomyomas:**

Removal of sessile myomas embedded within the myometrium generally requires both hysteroscopy and laparoscopy. The intramural portion is removed by shaving the tumor with the resectoscope loop; while the laparoscopist ascertain that the uterus is not being perforated.

Hysteroscopic resection should not be attempted if the myoma extends greater than 50% into the myometrial wall \(^{(113)}\).

**Complications:**
The most serious complication of hysteroscopic myomectomy is fluid overload, which can result in pulmonary edema, electrolyte disturbances and death. Fluid absorption should be calculated closely, as with all hysteroscopic surgery. Other potential complications include bleeding and uterine perforation (113).

**Outcome:**
Outcome after hysteroscopic resection is variable and depends upon the type of myoma and desired result. In one series of 108 women who underwent primary hysteroscopic removal of pedunculated, sessile and intramural myomas the myomas recurred in 27 subjects and 20 women had recurrent menorrhagia after a mean follow-up period of 41 months. The three year cumulative probability of conception in women with pedunculated, sessile and intramural lesions was 49, 36, and 33 percent respectively (114).

**Endometrial ablation:**
Endometrial ablation either alone or in combination with hysteroscopic myomectomy, may alleviate bleeding with minimal invasiveness in women with uterine leiomyomas who have completed childbearing. Although most case series of endometrial ablation have excluded women with significant myomas, one study that examined endometrial ablation with hysteroscopic myomectomy reported only an 8% risk for a second surgery after a mean of six year follow-up (111).

**Myolysis:**
Myolysis refers to laparoscopic coagulation of leiomyoma tissue (115). This technique is easier to master than resection which requires suturing. However, localized tissue destruction without repair may increase the chance of subsequent adhesion formation or rupture during pregnancy (116).
Myolysis combined with endometrial ablation is a more effective therapy than either procedure alone. A descriptive study that compared ablation alone with the combined procedures in women with menorrhagia found that the risk of a second surgery was 38 and 13 percent respectively (117).

**Uterine artery embolization:**

Uterine artery embolization (UAE) is an innovative technique based upon the hypothesis that control of myometrial arterial blood flow will control symptoms (118-120). One study found the technique was useful in controlling leiomyoma-related menorrhagia in approximately 90 percent of patients and pressure symptoms in 91 percent at 1 year after treatment; 10 percent required surgical intervention during the follow-up period (30). The mean reduction in uterine volume appears to be 40 to 60 percent (121-122, 30). However, mean volume reduction may be lower in women with only intramural myomas since submucous myomas are likely to be expelled vaginally after UAE and submucosal location is a strong predictor of volume reduction (122,123-125).

Other – Regulation of growth factor pathways is another area of innovative treatment. There is evidence that interferons can reverse the proliferative effects of bFGF on leiomyoma cells in culture (126). As an example, a woman undergoing treatment with interferon-alfa for hepatitis C had dramatic and sustained shrinkage of a uterine leiomyoma after seven months of therapy (127).

**Pregnancy:**

Uterine leiomyomas occur in approximately two percent of pregnant women and usually do not interfere with the course of pregnancy (128-129). Myomectomy during pregnancy should be avoided, if possible, because of
the risk for intraoperative hemorrhage and subsequent pregnancy loss (130-131). The procedure may be considered for symptomatic myomas that do not respond to conservative therapy, especially if the myoma is pedunculated and readily resectable (132-133).

**Disadvantages of myomectomy**

Although myomectomy is an effective therapy for menorrhagia and pelvic pressure, the disadvantage of this procedure is the significant risk that more leiomyomas will develop from new clones of abnormal myocytes. Five years after myomectomy, approximately 50 percent of patients will have myomas detected by ultrasound (134), and 11 to 26 percent will require a second surgery after the first myomectomy (135-137).

**Hysterectomy:**

Hysterectomy eliminates both current symptoms and the chance of recurrent problems from fibroids. For many women who have completed childbearing, this freedom from future problems provides an attractive option (63). As an example, a two year follow-up study of 1299 women who had undergone hysterectomy for benign conditions found that more than 90 percent noted significant reductions in symptom severity, depression, and anxiety levels, and an improvement in quality of life (13).

Hysterectomy may be performed either with or without oopherectomy without apparent sequelae with reference to myomas (13).

Patients with symptomatic uteri should be offered a trial of conservative management prior to hysterectomy. Symptoms of excessive uterine bleeding lasting longer than 8 days or bleeding either acutely or chronically to the point of anaemia are considered adequate indications for surgery. In addition, acute or severe abdominal pain, chronic abdominal or back pain, or pressure on contiguous organs to the point of discomfort is considered an
adequate indication for operative intervention\textsuperscript{(16)}.

The procedure may be performed via a midline or Pfannenstiel incision, depending on the patient’s body habitus, skeletal configuration, and the size and configuration of the uterine myomas. The same techniques are performed during hysterectomy for other reasons should be followed in the performance of hysterectomy for myomas\textsuperscript{(16)}.

**Future Directions:**

The biology of uterine fibroids has traditionally been explained in terms of steroid hormones; thus, all current medical therapies are based upon manipulation of these hormones. However, an expanded view of the biology of this benign tumor (e.g., the specific genes that are deregulated) may open new avenues of pharmaceutical intervention and ultimately lead to strategies for prevention\textsuperscript{(117)}.
Objectives

1- To find out factors which affect the type of operation done for myoma treatment.

2- To assess the range of complications and outcome associated with the two treatment modalities.
CHAPTER TWO
Patients and methods:

Study design:
A descriptive prospective, cross sectional, hospital based study.

Study period:
The study was carried out in the period from 15\textsuperscript{th} of September 2004 to the 15\textsuperscript{th} of March 2005.

Study area:
The study was conducted in three maternity units in three hospitals in Khartoum state:

1. Ribat University Hospital; the major hospital of police force in Sudan.
2. The Academy charity hospital in AlsaHafa area; where medical students of The Academy of medical sciences receive their clinical training.
3. Soba University hospital; the major hospital where Khartoum University supervises training of medical students and registrars.

Study population:
One hundred and fourteen women with uterine fibroids presented to the three hospitals where the study was carried out during the study period, were selected.

From the total 77 women had myomectomy and 37 women had abdominal hysterectomy as the modality of treatment. Patients were selected to the study after giving an informed consent. The type of treatment was decided by the treating doctor without previous knowledge of the study participation.
**Data collection:**

Data was collected by direct interview of the patients using questionnaire containing information about personal data, parity and present history of the patient.

Information about size, site and number of the fibroids in addition to the intraoperative findings and postoperative complications were collected from the treating doctor's records.

**Data analysis:**

The data was analyzed using the computer statistical programme SPSS and presented in tables and figures. The P-value at 85% confidence interval was used as the test of significance.
## Results

### Table 1

**Type of operation and age**

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Age group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;30</td>
<td></td>
</tr>
<tr>
<td>Myomectomy</td>
<td>14(18.20%)</td>
<td>77(100.00%)</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>0(0.00%)</td>
<td>37(100.00%)</td>
</tr>
<tr>
<td>Total</td>
<td>14(12.30%)</td>
<td>114(100.00%)</td>
</tr>
</tbody>
</table>

- Chi-square: 25.291
- P_value: 0.00
### Table 2

**Type of operation and marital status**

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Marital status</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Single</td>
<td>Married</td>
</tr>
<tr>
<td>Myomectomy</td>
<td>33 (42.9%)</td>
<td>39 (50.6%)</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>3 (8.1%)</td>
<td>27 (73.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>36 (31.6%)</td>
<td>66 (57.9%)</td>
</tr>
</tbody>
</table>

Chi-square : 15.373
P_value: 0.00
### Table 3
Type of operation and parity

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Parity</th>
<th></th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nulliparous</td>
<td>1</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Myomectomy</td>
<td>56</td>
<td>17</td>
<td>4</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>(72.7%)</td>
<td>(22.1%)</td>
<td>(5.2%)</td>
<td>(100.0%)</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>8</td>
<td>17</td>
<td>12</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>(21.6%)</td>
<td>(45.9%)</td>
<td>(32.4%)</td>
<td>(100.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>64</td>
<td>34</td>
<td>16</td>
<td>114</td>
</tr>
<tr>
<td></td>
<td>(56.15)</td>
<td>(29.8%)</td>
<td>(14.0%)</td>
<td>(100.0%)</td>
</tr>
</tbody>
</table>

Chi\_square: 29.610
P\_value: 0.00
### Table 4

**Type of operation and size of fibroid**

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Size of fibroid</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 12 weeks</td>
<td>12-16 weeks</td>
</tr>
<tr>
<td>Myomectomy</td>
<td>29 (37.7%)</td>
<td>32 (41.1%)</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>14 (37.8%)</td>
<td>15 (40.5%)</td>
</tr>
<tr>
<td>Total</td>
<td>43 (37.7%)</td>
<td>47 (41.2%)</td>
</tr>
</tbody>
</table>

Chi-square: 0.015  
P-value: 0.993
Table 5

Type of operation and number of fibroids

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Number of the fibroids</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Single</td>
<td>2_5</td>
</tr>
<tr>
<td>Myomectomy</td>
<td>27</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>(35.1%)</td>
<td>(45.5%)</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(45.9%)</td>
<td>(16.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>44</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>(38.6%)</td>
<td>(36.0%)</td>
</tr>
</tbody>
</table>

Chi-square: 10.01
P_value: 0.007
### Table 6

**Type of operation and site of fibroids**

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Subserous</th>
<th>Intramural</th>
<th>Submucous</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myomectomy</td>
<td>24 (31.2%)</td>
<td>42 (54.5%)</td>
<td>11 (14.3%)</td>
<td>77</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>12 (32.4%)</td>
<td>16 (43.2%)</td>
<td>9 (24.3%)</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>36 (31.6%)</td>
<td>58 (50.9%)</td>
<td>20 (17.5%)</td>
<td>114</td>
</tr>
</tbody>
</table>

Chi-square: 2.076  
P-value: 0.354
<table>
<thead>
<tr>
<th>Site of fibroid</th>
<th>Asymptomatic</th>
<th>Presenting symptoms</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Menstrual disorders</td>
<td>Pressure symptoms</td>
</tr>
<tr>
<td>Subserous</td>
<td>19 (52.8%)</td>
<td>3 (8.3%)</td>
<td>14 (38.9%)</td>
</tr>
<tr>
<td>Intramural</td>
<td>36 (100.0%)</td>
<td>11 (19.0%)</td>
<td>11 (19.0%)</td>
</tr>
<tr>
<td>Submucous</td>
<td>3 (5.2%)</td>
<td>15 (75.0%)</td>
<td>2 (10.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>58 (50.9%)</td>
<td>29 (25.4%)</td>
<td>27 (23.7%)</td>
</tr>
</tbody>
</table>

Chi-square: 36.562
P_value: 0.00


<table>
<thead>
<tr>
<th>Site of fibroid</th>
<th>Fertility</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Subserous</td>
<td>10 (43.5%)</td>
<td>13 (56.5%)</td>
</tr>
<tr>
<td>Intramural</td>
<td>15 (36.6%)</td>
<td>26 (63.4%)</td>
</tr>
<tr>
<td>Submucous</td>
<td>2 (14.3%)</td>
<td>12 (85.7%)</td>
</tr>
<tr>
<td>Total</td>
<td>27 (100.0%)</td>
<td>51 (65.4%)</td>
</tr>
</tbody>
</table>

Chi_square: 3.425  
P_value: 0.180
**Table 9**
Type of operation and hemoglobin concentration

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Hemoglobin concentration</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean Preoperative Hb</td>
<td>Mean Postoperative Hb</td>
</tr>
<tr>
<td>Myomectomy</td>
<td>74.63%</td>
<td>67.90%</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>78.90%</td>
<td>71.36%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>153.53%</strong></td>
<td><strong>139.26%</strong></td>
</tr>
</tbody>
</table>

Chi_square: 0.0018443

P_value: >0.05
**Table 10**

*Type of operation and need for blood transfusion*

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Need for transfusion</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No need</td>
<td>1_2 pints</td>
</tr>
<tr>
<td>Myomectomy</td>
<td>44</td>
<td>21</td>
</tr>
<tr>
<td>(57.1%)</td>
<td>(27.3%)</td>
<td>(15.6%)</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>(45.9%)</td>
<td>(32.4%)</td>
<td>(21.6%)</td>
</tr>
<tr>
<td>Total</td>
<td>61</td>
<td>33</td>
</tr>
<tr>
<td>53.5%</td>
<td>(28.9%)</td>
<td>(17.5%)</td>
</tr>
</tbody>
</table>

Chi-square: 1.335  
P_value: 0.513
### Table 11

**Type of operation and duration of hospital stay**

<table>
<thead>
<tr>
<th>Type of operation</th>
<th>Duration of hospital stay</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4-7 days</td>
<td>&gt; 7 days</td>
</tr>
<tr>
<td>Myomectomy</td>
<td>38</td>
<td>39</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>10</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>48</td>
<td>66</td>
</tr>
</tbody>
</table>

Chi-square: 5.109  
P_value: 0.024
<table>
<thead>
<tr>
<th>Type of operation</th>
<th>No complications</th>
<th>Postoperative complications</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Fever</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Myomectomy</td>
<td>73 (94.8%)</td>
<td>2 (2.6%)</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Abdominal hysterectomy</td>
<td>31 (83.8%)</td>
<td>5 (13.5%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>104 (91.2%)</td>
<td>7 (6.1%)</td>
<td>1 (0.9%)</td>
</tr>
</tbody>
</table>

Chi-square: 5.944
P_value: 0.114
Figure 1

Distribution of type of the operation:

- Myomectomy: 33%
- Abdominal hysterectomy: 67%
Figure 2:

Frequency of infertility:
Figure 3:

◊Frequency of duration of infertility:
Figure 4:

**Frequency of presenting symptoms:**
Figure 5:

Frequency of past Obstetric and Gynecological history:
Figure 6

Frequency of type of anaesthesia:

- General anaesthesia: 85%
- Spinal anaesthesia: 15%
Results

Out of one hundred and fourteen women with uterine fibroids included in the study 77 women (67.5%) had myomectomy as the modality of treatment while 37 women (32.5%) had abdominal hysterectomy. Figure 1.

Of the women treated with myomectomy 18.2% (14 women) were less than 30 years old while no woman with abdominal hysterectomy was in that age group. 79.2% (61) of women who were treated by myomectomy were between 30 to 45 years compared to 25 women (67.5%) of women with abdominal hysterectomy. Two women with myomectomy (2.6%) were more than 45 years old compared to 12 women (32.4%) with abdominal hysterectomy. Table 1.

Comparing women treated with myomectomy to those treated with abdominal hysterectomy, 33 women with myomectomy (42.9%) were single women compared to 3 women with abdominal hysterectomy (8.1%). 39 married women (50.6%) had myomectomy while 27 (73.0%) married women had abdominal hysterectomy. Five women (6.5%) with myomectomy and 7 women (18.9%) with abdominal hysterectomy were widows or divorced women. Table 2.

Table 3 shows the comparison between hysterectomy and myomectomy in regards to parity. 56 women with myomectomy (72.7%) were nulliparous compared to 8 women (21.6%) with abdominal hysterectomy. 17 women (22.1%) with myomectomy and 17 (45.9%) with hysterectomy had 1 - 4 children. Women with more than 4 children were 4 (5.2%) treated with myomectomy compared to 12 women (32.4%) treated with abdominal hysterectomy. Table 3.
Out of the whole population, it was found that 27 women (23.7%) were infertile compared to 51 fertile women (44.7%). Single women were 36 comprising 31.6% of population. Figure 2.

Looking at the duration of infertility in the infertile population. Less than 2 years infertility was found in 5.3% of women (6 women) while 11 women (9.6%) had infertility for 2 to 5 years. More than 5 years infertility was found in 10 of all women studied (8.8%). Figure 3.

Figure 4 describes the presenting symptoms in the population. Asymptomatic women were 58 women comprising 50.9% of population, women with menstrual disorders were 29 women (25.9%) and those with pressure symptoms were 27 women (23.7%) of all women. Fig 4.

Considering past obstetrics and gynaecological history it was found that 99 of all women in the study (86.8%) had no past obstetrics or gynaecological history, 13 women (11.4%) had past history of myomectomy while 2 women (1.8%) had past history of caesarean section. Figure 5.

The size of the fibroids was less than 12 weeks in 29 women with myomectomy (37.7%) and in 14 women (37.8%) with abdominal hysterectomy. 32 women with myomectomy (41.1%) had fibroids ranging between 12 to 16 weeks compared to 15 women (40.5%) with abdominal hysterectomy. More than 16 weeks fibroids were found in 16 women (20.8%) with myomectomy and in 8 women (21.6%) with abdominal hysterectomy. Table 4.

Single fibroid was found in 27 women (35.1%) with myomectomy and in 17 (45.9%) of those with abdominal hysterectomy. Two to five fibroids were found in 35 (45.5%) women with myomectomy compared to 6 women (16.2%) with abdominal hysterectomy. More than 5 fibroids were found in
15 women (19.5%) with myomectomy and in 14 women (37.8%) with abdominal hysterectomy. Table 5.

Comparing momentum with abdominal hysterectomy it was found that of the women treated by myomectomy, 24 women (31.2%) had subserous fibroids, 42 women (54.5%) had intramural fibroids and 11 women (14.3%) had submucous fibroids. In comparison 12 women with abdominal hysterectomy (32.4%) had subserous fibroids, 16 (43.2%) women had intramural fibroids and 9 women (24.3%) had submucous fibroids. Table 6.

Table 7 shows the site of fibroids in relation to the presenting symptoms. It was found that 19 women (52.8%) with subserous fibroids were asymptomatic compared to 36 women (62.1%) with intramural fibroids and 3 women (5.2%) of those with submucous fibroids. Menstrual disorders occurred mostly in women (15) with submucous fibroids (75.0%), in 11 women (19.0%) with intramural fibroids and in 3 women (8.3%) with subserous fibroids. While pressure symptoms occurred mostly (38.9%) with subserous fibroids (14 women), in 11 women (19.0%) with intramural fibroids and in 2 women (10.0%) of those with submucous fibroids.

When considering the site of the fibroids in relation to fertility status it was found that 2 women (14.3%) with submucous fibroids were infertile compared to 15 women with intramural fibroids (36.6%). In fertile women 10 had subserous fibroids (43.5%). 13 of the fertile women had subserous fibroids (56.5%), 26 (63.4%) had intramural fibroids and 12 women (85.7%) had submucous fibroids. Table 8.

There was more intraoperative blood loss associated with abdominal hysterectomy than with myomectomy. Table 9. The mean preoperative Hb concentration was 74.63% in women with myomectomy compared to 78.90% in those with abdominal hysterectomy. In comparison, the mean
postoperative Hb concentration was 67.90% in myomectomy and 71.36% in hysterectomy. There was a difference in preoperative and postoperative Hb concentration of 6.72% in women with myomectomy compared to 7.54% in those with hysterectomy. Table 9.

Type of anaesthesia used for operation was general anaesthesia in 97 women comprising 85.1% of population while in the remaining 17 women (14.9%) spinal anaesthesia was used. Figure 6.

Forty-four women with myomectomy (57.1%) did not need blood transfusion compared to 17 women (45.9%) with abdominal hysterectomy. 21 (27.3%) women with myomectomy and 12 (32.4%) women with abdominal hysterectomy received 1 to 2 pints of blood while 12 women (15.6%) with myomectomy and 8 (21.6%) with abdominal hysterectomy received more than 2 pints of blood. Table 10.

Duration of hospital stay ranged between 4 to 7 days in 38 women (49.4%) with myomectomy and more than 7 days in 39 women (50.6%). Of women treated by abdominal hysterectomy, 10 women (27.0%) stayed in hospital for 4 to 7 days, while 27 women (73.0%) stayed more than one week. Table 11.

No postoperative complications occurred in 73 women (94.8%) of women with myomectomy and in 31 women (83.8%) with abdominal hysterectomy. Two women treated by myomectomy had fever, one woman (1.3%) had abdominal pain and one woman (1.3%) had bleeding postoperatively. In comparison 5 women (13.5%) treated by abdominal hysterectomy had fever, no woman had abdominal pain and one woman (2.7%) had bleeding. Table 12.
CHAPTER
FOUR
Discussion

One hundred and fourteen women with uterine fibroids who presented to the three hospitals where the study was carried out were included in this study. The modality of treatment applied to them was studied comparing myomectomy to abdominal hysterectomy.

In this study myomectomy was the commonest used modality of treatment (67.5%).

The majority of women (75.4%) were between 30 to 45 years old. Compared to the literature, fibroids were found in 20% to 25% of women aged over 35 years \(^{(2)}\). It was found that abdominal hysterectomy was more common in women over 45 years while myomectomy was common in those less than 30 years. This may reflect the fact that women more than 45 years usually had completed their families and had no desire for more childbearing. Vessey MP found that hysterectomy generally tended to increase with age \(^{(133)}\). In a study done by Iverson et al it was found that there were significant differences between the two groups for average age (hysterectomy 39.2 years, myomectomy 34.4 years; mean difference 4.8, 95% confidence interval [CI] of difference 3.7-5.9) \(^{(80)}\).

Hillis et al found that myomectomy is the first option for women who desire future pregnancies or otherwise wish to retain their uterus or improve pregnancy outcome after repetitive miscarriages \(^{(79)}\).

In this study, comparing women treated with myomectomy to those treated with abdominal hysterectomy it was found that 42.9% of women with myomectomy were single women compared to 8.1% of women with
abdominal hysterectomy. This may be in part due to the more conservative approach of management applied to single women in our community. This may also be applied to married women: 39 women (34.2% of population) were married and were treated with myomectomy compared to 27 married women (23.7% of population) treated with abdominal hysterectomy. Marital status per se does not seem to affect the decision of myomectomy or abdominal hysterectomy. It is the future fertility plans which affect such a decision. The reverse is true for widows and divorced women where hysterectomy was the most commonly used type of management (used in 18.9% of women compared to 6.5% for myomectomy).

Hysterectomy eliminates both current symptoms and the chance of recurrent problems from fibroids. For many women who have completed childbearing, this freedom from future problems provides an attractive option\(^{(134)}\).

It was found that the majority (56.1%) of women included in the study were nulliparous while 43.9% of them are parous women. This is consistent with the concept that parity (having one or more pregnancies extending beyond 20 weeks) decreases the chance of fibroid formation\(^{(7,9)}\).

In this study 87.5% of nulliparous women were treated with myomectomy while the rest of them had hysterectomy. Women with more than four children had hysterectomy (75% of them) more than myomectomy (25%). This may also support the above mentioned concept of conservative management for women who wish to preserve child bearing potential or enhance it.
Fertile women were noticed to be more in the whole population (44.7%) compared to infertile ones (23.7%). Single women comprise 31.6% of population. These were not included in the fertility analysis.

As mentioned in the literature it is estimated that infertility is the major presenting secondary feature in around 27% of women with fibroid. The mechanism whereby fibroid adversely affect conception is unclear, but it is likely to be mechanical by virtue of cornual occlusion or by distortion of the cavity, preventing implantation\(^{(140)}\)

In this study when site of the fibroids was analyzed in connection with the fertility status, it was found that 55.6% of infertile women had intramural fibroids compared to 7.4% with submucous fibroids and 37% with subserous fibroids. It is mentioned in the literature that the role of intramural leiomyomas in infertility is controversial; some studies suggest myomas are sources of infertility \(^{(47)}\); while more recent reports from women undergoing in vitro fertilization suggest they play a role \(^{(48\_50)}\).

Garcia et al founded that the risk of infertility is increased when the endometrial cavity is distorted by submucous leiomyomas \(^{(46)}\). It may result from mechanical obstruction or occlusion of the fallopian tubes and it may prevent implantation of a fertile ovum \(^{(3)}\).

Considering the past obstetric and gynecological history it was found that 11.4% of all women had past history of myomectomy. This may reflect the recurrence rate of fibroids. In one study the recurrence rate of fibroid was 15%. Overall 10% of the women required further pelvic surgery, usually hysterectomy for recurrent or continuing symptoms following myomectomy. \(^{(136)}\)
In another study the 10 years recurrence rate was as high as 27%, the outcome being more favourable for those who achieved a pregnancy compared with those who did not\(^{(137)}\).

This different recurrence rate in these studies may be due to the difference in the duration of follow up.

Regarding the presenting symptoms it was found that 50.9% of women were asymptomatic. This is consistent with what is mentioned in the literature that most small myomata, and some larger ones, are symptomless and are only detected during a routine examination\(^{(7)}\) and that uterine fibroids, which eventually develop in more than 50% of women, are usually asymptomatic\(^{(138)}\).

Menstrual disorders occurred in 25.4% of the study population. Compared to literature, it is mentioned that the most common symptom associated with leiomyoma is abnormal uterine bleeding\(^{(16)}\).

In this study pressure symptoms occurred in 23.7% of study population. This is close to what was mentioned in the literature, that pressure symptoms may be reported in up to 30% of patient with uterine myoma\(^{(16)}\).

When considering the site of the fibroids in regards to the presenting symptoms it was found that there is significantly more menstrual disorders associated with submucous fibroids (75.0%) compared to subserous and intramural fibroids and more pressure symptoms associated with subserous fibroids (38.9%).
Women with large fibroids of more than 16 weeks uterine size were treated with abdominal hysterectomy (21.6%) more than with myomectomy (20.8%). This may be due to the fear of massive blood loss associated with large or multiple fibroids. This finding is consistent with Iverson et al study where the mean fundal height in patients who underwent hysterectomy was 15.2 weeks compared to 11.5 weeks for myomectomy\(^{(80)}\).

There was no difference between myomectomy and hysterectomy regarding treatment of women with small fibroids of less than 12 weeks size.

As mentioned in the literature, it is rare that only single myoma develops, they are usually multiple and that they may be very numerous\(^{(4)}\). In this study single fibroid was found in 38.6% of all women, while 61.4% had more than one fibroid.

Abdominal hysterectomy was associated with more intraoperative blood loss compared to Myomectomy. This is evident by the more decrease in the mean postoperative Hb in the former (7.54% vs. 6.73%).

Blood transfusion was more in women treated with hysterectomy than those with myomectomy. 42.9% of women with myomectomy and 54% of women with abdominal hysterectomy received blood transfusion. These results were consistent with the study done by Iverson et al; they estimated a blood loss of 796 ml associated with abdominal hysterectomy compared to 464 ml in myomectomy\(^{(80)}\).

The higher transfusion rate associated with hysterectomy may be due to more experience in doing myomectomy than hysterectomy especially by the junior staff.
Duration of hospital stay ranged between 4 to 7 days in 49.4% of women with myomectomy and in 27.0% of women treated by abdominal hysterectomy. While 50.6% of women treated by myomectomy and 73.0% of those with abdominal hysterectomy stayed in hospital for more than one week. This long hospital stay compared to Hutchins Study (2 to 3 days) may be attributed to the fact that in our hospitals as general we tend to keep patients with major surgeries for five days or more due to the use of midline longitudinal incision and closure with interrupted silk stitches. (139).

The overall complication rate was 8.2% of population. Women with myomectomy had more postoperative complications (94.8% of them) than those with abdominal hysterectomy (83.8% of them). Extensive tissue damage associated with myomectomy may explain this.
Conclusion

Fibroids are the commonest solid tumours of female genital tract.
In this study myomectomy was the commonest used modality of treatment.
The majority of women were between 30 to 45 years old and the majority of them were nulliparous.
Fertile women were noticed to be more in the whole population than infertile one.
Nearly half of the women were asymptomatic, while menstrual disorders occurred in approximately a quarter of the study population.
Women with fibroids of more than 16 weeks size were treated with abdominal hysterectomy more than with myomectomy.
Most of the women had more than one fibroid.
The recurrence rate of fibroids was close to that in the literature.
Abdominal hysterectomy was associated with more intraoperative blood loss and more blood transfusion than myomectomy.
Women with myomectomy had more postoperative complications than those with abdominal hysterectomy.
**Recommendations**

- Myomectomy should be the treatment of choice for women with symptomatic uterine fibroids who desire future fertility but it carries the risk of recurrence.
- Hysterectomy eliminates both current symptoms and the chance of recurrence. It should be used for women who completed their families.
- Women should be counseled that hysterectomy is associated with less postoperative complication rate compared to myomectomy.
- Adequate amount of blood should be prepared for both hysterectomy and myomectomy.
- Duration of hospital stay should be shortened in our hospitals taking in consideration more objective reasons for determination of postoperative hospital stay. Transverse pfannenstiel incision with subcutaneous closure of the wound should be advised in women with small uteri.


20. Kurman RJ, Norris HJ. Mesenchymal tumors of the uterus. VI Epithelioid smooth muscle tumors including leiomyoblastoma and


27. Lee BS, Stewart EA, Sahakian M, Nowak RA. Interferon-alpha is a potent inhibitor of basic fibroblast growth factor-stimulated cell


32. Treloar SA, Martin NG, Dennerstein L. Pathways to hysterectomy:


40. Thompson JD, Rock JA. Leiomyomata uteri and myomectomy. In:


47. Surrey ES, Lietz AK, Schoolcraft WB. Impact of intramural leiomyomata in patients with a normal endometrial cavity on in vitro


54. Koike T, Minakami H, Kosuge S. Uterine leiomyoma in


62. ACOG. American College of Obstetricians and Gynecologists. Surgical alternatives to hysterectomy in the management of


103(Suppl 14):18.


104. Mais V, Ajossa S, Guerriero S. Laparoscopic versus abdominal


120. Hutchins FL Jr, Worthington-Kirsch, R, Berkowitz, RP. Selective


Appendix
Myomectomy versus abdominal hysterectomy in management of uterine fibroid

(Questionnaire)

Serial No: ............

1. Age:
   1. <30  2. 30 – 45  3. >45 years

2. Marital status:
   1. single  2. Married  3. Widow / divorce

3. Parity:
   1. Nulliparous  2. 1-4  3. >4

4. Infertility:
   1. yes  2. no

   If yes duration of infertility:
   1. <2 years  2. 2-5 years  3. >5 years

5. C/O:
   1. a symptomatic
   2. Menstrual disorders
   3. Pressure symptoms

6. Post history:
   1. No previous gynecological surgery
   2. previous Myomectomy
   3. Previous c/s
O/E:

7. Size of the fibroid.
   1. <12 weeks  2. 12-16 weeks  3. >16 weeks

8. Number of the fibroid.
   1. single  2. 2-5  3. >5

9. Site of the fibroid.
   1. subserous  2. Intramural  3. Submucous

10. Type of anesthesia
    1. General  2. Spinal

11. Hb % preoperative.

12. Hb % postoperative.

13. Need for blood transfusion:
    1. No  2. 1-2 pints.  3. >2pints.

14. Hospital stay:
    1. 4-7days  2. >7days

15. Postoperative complications:

16. Type of operation
    1. myomectomy  2. Abdominal hysterectomy.