

Uterine Leiomyoma (Fibroids)

What is Leiomyoma ?

Leiomyoma is a non cancerous tumour(does not spread to other parts of body,**benign**) that grows in smooth muscle tissues, in our case its in uterus.And can vary in size from a tiny seed to large mass that distorts the uterus.

Found in Uterus in this case ,Can also develop in stomach , intestines, skin or blood vessels.

Usually harmless and slow-growing.Might cause pain, pressure or bleeding if it grows larger.

Types of Uterine Fibroids

Fibroids are classified based on where they grow in the uterus:

- 1 Intramural fibroids** – Grow inside the muscular wall of the uterus. (Most common)
- 2 Subserosal fibroids** – Grow on the outer surface of the uterus and may press on nearby organs.
- 3 Submucosal fibroids** – Grow inside the uterine cavity, causing heavy bleeding and fertility problems.
- 4 Pedunculated fibroids** – Grow on a stalk-like structure either inside or outside the uterus.

Causes and Risk Factors

Although the exact cause is unknown, the following factors contribute to fibroid development:

1 Hormones (Estrogen & Progesterone)

- Estrogen and progesterone help fibroids grow.
- During pregnancy, fibroids may enlarge due to increased hormone levels.
- After menopause, fibroids often shrink due to decreased estrogen.

Estrogen is the primary female sex hormone responsible for the development and regulation of the female reproductive system and secondary sexual characteristics.

Progesterone is a hormone that prepares the body for pregnancy and maintains the menstrual cycle.

2 Genetic Factors

- Family history increases the risk.
- If your mother or sister had fibroids, you are more likely to develop them.

What is Familial Leiomyoma?

Familial leiomyoma refers to a genetic condition where multiple leiomyomas (benign smooth muscle tumors) develop in different parts of the body. This condition is inherited in families, meaning it has a strong genetic link.

One of the types Include:

Uterine Familial Leiomyomatosis (Hereditary Uterine Fibroids)

- Involves the growth of multiple fibroids (leiomyomas) in the uterus.
- Affects women at an earlier age than sporadic (non-genetic) fibroids.
- Often larger and more numerous than regular uterine fibroids.
- Symptoms: Heavy bleeding, pelvic pain, infertility, and pregnancy complications.

Cutaneous Familial Leiomyomatosis (Skin Leiomyomas)

- Involves smooth muscle tumors on the skins, commonly on the trunk, arms, and legs.
- Typically appear as small, firm, reddish-brown bumps.
- Can cause pain, especially in response to cold or touch.

Combination: Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC)

- Rare genetic syndrome caused by a mutation in the FH (Fumarate Hydratase) gene.
- Leads to both skin and uterine leiomyomas and increases the risk of kidney cancer.
- Needs regular screening for renal cancer in affected individuals.

3 Growth Factors

- Certain substances that help tissues grow, like insulin-like growth factors, may play a role.

4 Lifestyle & Other Risk Factors

- Obesity – Higher fat levels increase estrogen production.
- Diet – High consumption of red meat may increase risk, while green vegetables may lower it.
- Alcohol & caffeine – Can increase estrogen levels, potentially influencing fibroid growth.
- Pregnancy & childbirth – Can protect against fibroids or shrink them over time.

Whats RCC ?

Renal Cell Carcinoma ,is the most common type of kidney cancer, originating from the renal tubules.

Renal Tubules (Function):

The renal tubules are small tube-like structures in the nephrons of the kidney. They play a key role in filtering blood, reabsorbing essential substances, and removing waste to form urine.

Genetics of Leiomyoma

How Cell Division Leads to Leiomyoma (Uterine Fibroids)?

Uterine leiomyomas (fibroids) develop due to uncontrolled cell division in the smooth muscle cells of the uterus. Normally, cell division (mitosis) is tightly regulated, but genetic mutations, hormonal influence, and growth factors disrupt this balance, leading to fibroid formation.

Normal Cell Division (Mitosis) in Uterine Cells

In healthy uterine smooth muscle cells, mitosis follows these steps:

G1 Phase: The cell grows and prepares for DNA replication.

S Phase: DNA is copied.

G2 Phase: The cell prepares for division.

M Phase (Mitosis): The cell splits into two identical daughter cells.

Regulation: Controlled by cell cycle checkpoints, tumor suppressor genes (e.g., TP53), and growth factors.

How Cell Division Leads to Fibroids ?

Mutations in genes like MED12 and HMGA2 disrupt normal mitosis.

Excess estrogen and progesterone stimulate uncontrolled cell division.

Growth factors (TGF- β , IGF-1) promote fibroid formation.

ECM accumulation provides structural support for excessive growth.

End Result: Uncontrolled smooth muscle cell proliferation forms a fibroid mass.

Abnormal Cell Division in Leiomyoma

Leiomyomas occur when genetic mutations and hormonal imbalances disrupt normal cell cycle regulation, causing excessive and uncontrolled proliferation.

A) Mutations Affecting Cell Cycle Regulation

MED12 Gene Mutation (70%)

- MED12 controls transcription in RNA polymerase II.
- A mutation disrupts cell division regulation, leading to excessive growth.

HMGA2 Overexpression (10-15%)

- Enhances cell proliferation by affecting chromatin structure.

FH Mutation (HLRCC Syndrome)

- Causes metabolic changes, leading to excessive cell proliferation.

B) Hormonal Influence (Estrogen & Progesterone)

- Estrogen & progesterone stimulate smooth muscle growth and increase production of growth factors (EGF, TGF- β , IGF-1).
- These override normal cell cycle checkpoints, allowing uncontrolled mitosis.

C) Growth Factors and Extracellular Matrix (ECM) Changes

- **TGF- β (Transforming Growth Factor-Beta)** promotes excessive fibrous tissue formation.
- Increased ECM components (collagen, fibronectin) create a dense environment that traps proliferating cells, forming a fibroid mass.

Role of Karyotype in Leiomyoma (Fibroids)

A **karyotype** is a test that examines the number and structure of chromosomes in cells. In uterine leiomyomas (fibroids), karyotyping helps identify genetic abnormalities that contribute to tumor growth.

Why is Karyotyping Important in Fibroids?

Detects Chromosomal Changes – Many fibroids have genetic abnormalities, which can be seen in a karyotype.

Helps Understand Tumor Development – Genetic mutations cause uncontrolled cell division.

Differentiates Between Fibroid Types – Some fibroids grow faster due to specific chromosomal abnormalities.

How Karyotyping is Done for Fibroids?

- 1 Sample Collection** – Uterine tissue is obtained (biopsy or surgery).
- 2 Cell Culture** – Cells are grown in the lab.
- 3 Chromosome Staining** – Special dyes highlight chromosomes.
- 4 Microscopic Analysis** – Chromosome changes are identified.

Treatment for Uterine Fibroids

- No treatment if there are no symptoms.
- Medications like hormonal therapy to shrink fibroids.
- **Surgery**
 - **Myomectomy** (removal of fibroids, preserving the uterus) – for women who want to have children.
 - **Hysterectomy** (removal of the uterus) – for severe cases or when pregnancy is not a concern.

Clinical examination

Urine Examination (Urinalysis) in Leiomyoma

A urine test is usually performed to:

Rule out urinary tract infections (UTIs) – Fibroids pressing on the bladder can cause urinary frequency or urgency, which mimics a UTI.

Check for hematuria (blood in urine) – Large fibroids may compress the bladder or ureters, causing bladder irritation or mild bleeding.

Assess kidney function – Obstructive fibroids can sometimes cause hydronephrosis (urine backup into the kidneys), affecting kidney function.

How is it Done?

A midstream urine sample is collected.

- The sample is analyzed for:
 - **Red blood cells (RBCs)** – To detect bleeding
 - **White blood cells (WBCs)** – To check for infection
 - **Protein & glucose** – To rule out other medical conditions

Urinalysis Findings in Fibroid Cases:

- **Normal findings** in most cases
- **Blood in urine (hematuria)** if fibroids are pressing on the bladder
- **Signs of UTI (bacteria, WBCs, nitrates)** if infection is present due to urinary retention.

Endometrial Sampling (Biopsy/Curettage) in Leiomyoma

Endometrial biopsy or dilatation and curettage (D&C) is done in cases where abnormal uterine bleeding (AUB) is present. It helps to:

Differentiate fibroids from endometrial hyperplasia or cancer.

Identify hormonal imbalances affecting the endometrium.

Confirm coexisting conditions like endometrial polyps.

How is it Done?

- A small tissue sample is collected from the lining of the uterus (endometrium) using:
 - Pipelle biopsy (thin tube inserted into the uterus)
 - D&C procedure (scraping of the uterine lining)
- The sample is sent for histopathological analysis to check for abnormal cell growth.

Endometrial Biopsy Findings in Fibroid Cases:

- **Normal endometrium** (most common)
- **Endometrial hyperplasia** (thickened lining due to hormonal imbalance)
- **Atrophic endometrium** (thinning of the lining, common in postmenopausal women)
- **Endometrial cancer (rare but important to rule out)**

Urine Examination – Helps rule out infections, kidney issues, or bladder compression.

Endometrial Sampling – Helps evaluate abnormal bleeding and rule out hyperplasia or cancer.