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Chapter

Bleeding

Kizito Omona

Abstract

Fibroid, also called leiomyomas, is common tumor of the uterus. Usually, women of reproductive age are at risk of getting it. However, majority of these women develop fibroid (s) by the age of 50 years. This condition usually causes painful and unpleasant symptoms such as; heavy bleeding, prolonged periods, inter-menstrual bleeding, abdominal pain and cramps, anemia, pelvic pain and pain during sexual intercourse, among others. Abnormal bleeding, such as bleeding that occurs with fibroids and heavy periods, often lasts more than 10 days per month. This fibroid symptom involves persistent bleeding between cycles, which can severely impact one's quality of life. Abnormal bleeding, especially in fibroids, can be taken as missing three or more periods in a woman who had been having regular monthly period, or periods that last less than 21 days or more than 35 days apart from each other. Another indication of an abnormal period is bleeding through multiple pads and tampons in a short amount of time.

Keywords: per vaginal bleeding, abnormal bleeding, normal bleeding, menstrual bleeding, menstrual cycle

1. Introduction

In a normal adult human – female, menstrual cycle occurs to provide for release of oocyte, thus preparing the uterus for any possible pregnancy [1].

Thus, menstruation is a woman's normal monthly per vaginal bleeding, usually called "monthly period." When a woman menstruates, her body discards the monthly build-up of the lining of the uterus. The resultant blood, also called menstrual blood, and uterine tissues flow from the uterus through the cervix and then into the vagina and eventually out of the body [2]. In other words, menstruation is the cyclic and orderly sloughing off of the uterine lining which occurs in response to the interactions of hormones produced by the hypothalamus, pituitary and ovaries [3].

Menstrual cycle is, thus, divided into three phases. These are follicular or proliferative phase, ovulation and luteal or secretory phase. The number of days between the first day of menstrual bleeding of a woman's cycle to the onset of menses of the next cycle is referred to as 'the length of a menstrual cycle'. The average duration of a menstrual cycle is usually 28 days. However, some women may have shorter cycle of 21 days. Such women are referred to as 'polymenorrheic women'. Some women also have longer cycle of 35 days or more. These are called oligomenorrheic women [3]. Thus, the complete cycle may last anywhere from 21 days to 35 days with an average duration of 28 days for most women.

Menstruation begins at puberty, usually between ranging 10 to 16 years of age of a normal girl child. It ends at menopause, corresponding to average age of 45 to 55 years of a normal adult female [1].

Ordinarily, the typical volume of blood lost during menstruation is approximately 30 milliliters (mL). Any amount of blood lost during menstruation which is greater than 80 mL is considered abnormal [4].

2. Physiology of normal uterine bleeding

There are four major circulating hormones involved in the menstrual cycle. These hormones are; follicle stimulating hormones (FSH), luteinizing hormones (LH), estradiol (estrogen) and progesterone. The concentrations of these hormones in blood vary and their levels provide characteristic changes during the menstrual cycle [5]. In particular, the body makes three main types of estrogen; estrone (E1), estradiol (E2) and estriol (E3). E1 is the only estrogen the body makes after menopause. E2 is the most common type in women of childbearing age whereas E3 is the main estrogen during pregnancy [6].

The menstrual cycle is triggered by the gonadotropin-releasing hormone (GnRH) pulse generator in the hypothalamus. The GnRH pulse generator then releases gonadotropin-releasing hormone (GnRH) [7]. This GnRH in turn stimulates the synthesis and release of the gonadotropins, luteinizing hormones (LH) and follicle stimulating hormones (FSH), from the anterior pituitary gland [5]. LH and FSH exert their effects in the ovaries. There are two types of cells responsible for hormone production within the ovarian follicle; theca cells and granulosa cells. LH acts on theca cells to produce progesterone and androstenedione. The enzyme involved is cholesterol desmolase. Upon secretion of androstenedione, the hormone diffuses to granulosa cells. FSH then stimulates the granulosa cells to convert androstenedione to testosterone and eventually 17-beta-estradiol. The enzyme involved is aromatase. The levels of 17-beta-estradiol or progesterone increases accordingly, depending on the phase of the menstrual cycle. This increase triggers a negative feedback back to the anterior pituitary to lower the levels of FSH and LH which are being produced and subsequently, the levels of 17-beta-estradiol and progesterone produced. The only exception occurs during ovulation, in which case, once a critical amount of 17-beta-estradiol is produced it provides positive feedback to the anterior pituitary instead of a negative feedback [5, 6]. This positive feedback results in increased amounts of FSH and LH, hence the LH surge bringing about ovulation [1].

The onset of the menstrual cycle, or menarche, usually at 10–16 years, begins at puberty and ceases at menopause, usually 45–55 years. The cycle has 3 phases: follicular or proliferative phase, ovulation and luteal or secretory phase [1, 5].

Follicular Phase: Usually, the first phase of the menstrual cycle is the follicular or proliferative phase. The phase is characterized by menstruation, resulting from shedding off of the initially thickened endometrial lining following failed fertilization or implantation. It occurs from day zero to day 14 of the menstrual cycle (see **Figures 1** and **2**), based on the average duration of 28 days cycle. There is usually variability in the length of menstrual cycle and this is due to variations in the length of the follicular phase. The main hormone during this phase is estrogen, in particular 17-beta-estradiol [1, 5] from the ovary coupled with follicle stimulating hormone (FSH), released from anterior pituitary gland. Upon release from anterior pituitary, FSH and LH slowly rise in levels and cause the growth of follicles on the surface of the ovary. This process prepares the egg for ovulation. As the follicles grow, they begin releasing estrogens and a low level of progesterone. These ovarian hormones then inhibit further release of GnRH from the hypothalamus, in a

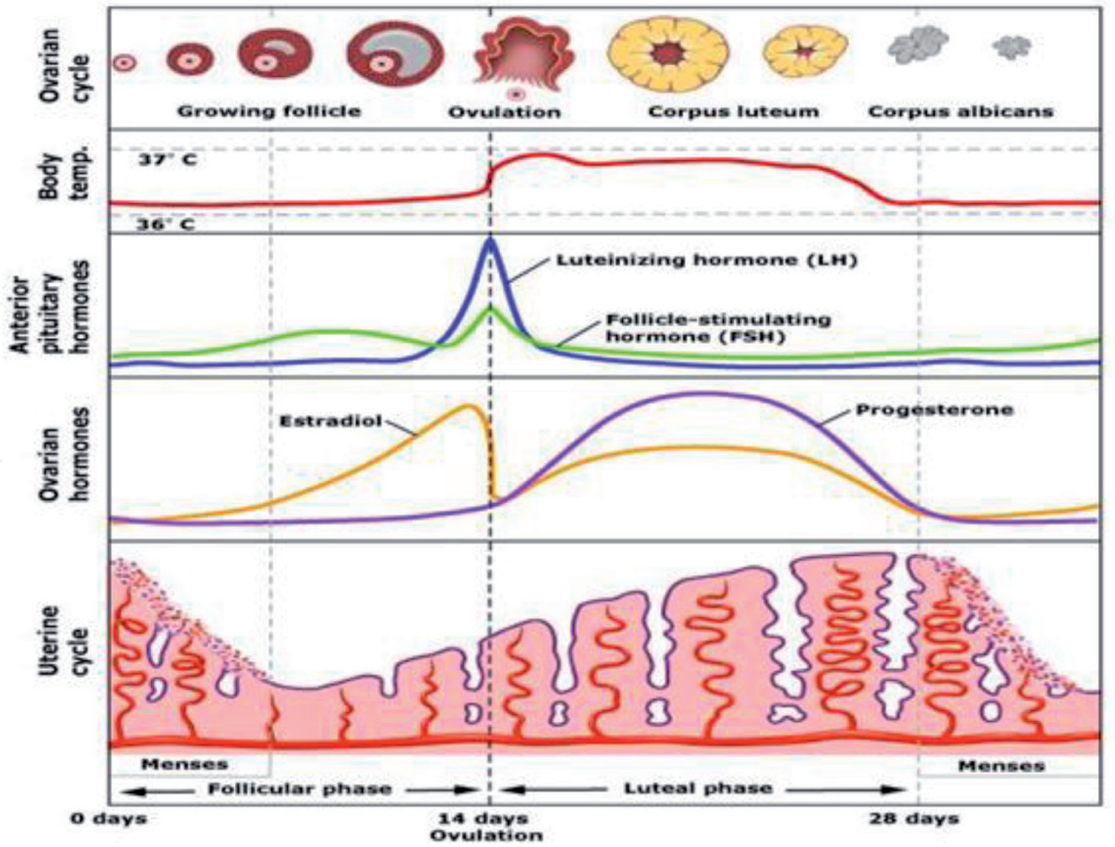


Figure 1.
Hormonal changes in the menstrual cycle.

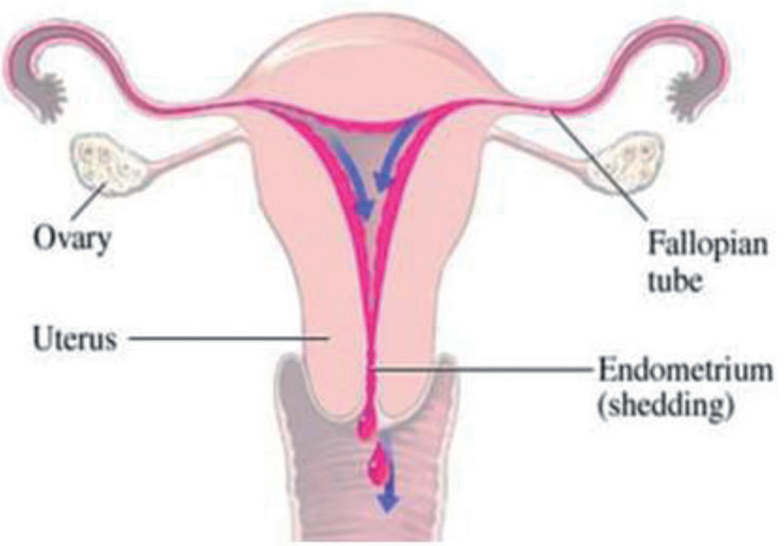


Figure 2.
Menstrual flow.

negative feedback process (See **Figure 3**). Thus, as the follicular phase progresses to the end, the increased amounts of 17-beta-estradiol will provide negative feedback to the anterior pituitary.

Due to the rise of FSH during the first days of the menstrual cycle or follicular phase, several ovarian follicles are stimulated. These ovarian follicles compete with each other for dominance. The follicle that reaches maturity is called a Graafian

follicle. During follicular phase, estrogen suppresses production of luteinizing hormone (LH) from the pituitary gland (**Figures 4** and **5**) [5].

Ovulation phase: Ovulation phase comes next. Ovulation occurs 14 days later after the first day of menstruation [1]. This means that with an average 28-day cycle, ovulation occurs on day 14 (see **Figure 1**).

At the end of the proliferative phase, 17-beta-estradiol (E2) levels are high due to the follicle maturation. During the follicular phase, estrogen suppresses production of luteinizing hormone (LH) from the pituitary gland but in this phase it stimulates

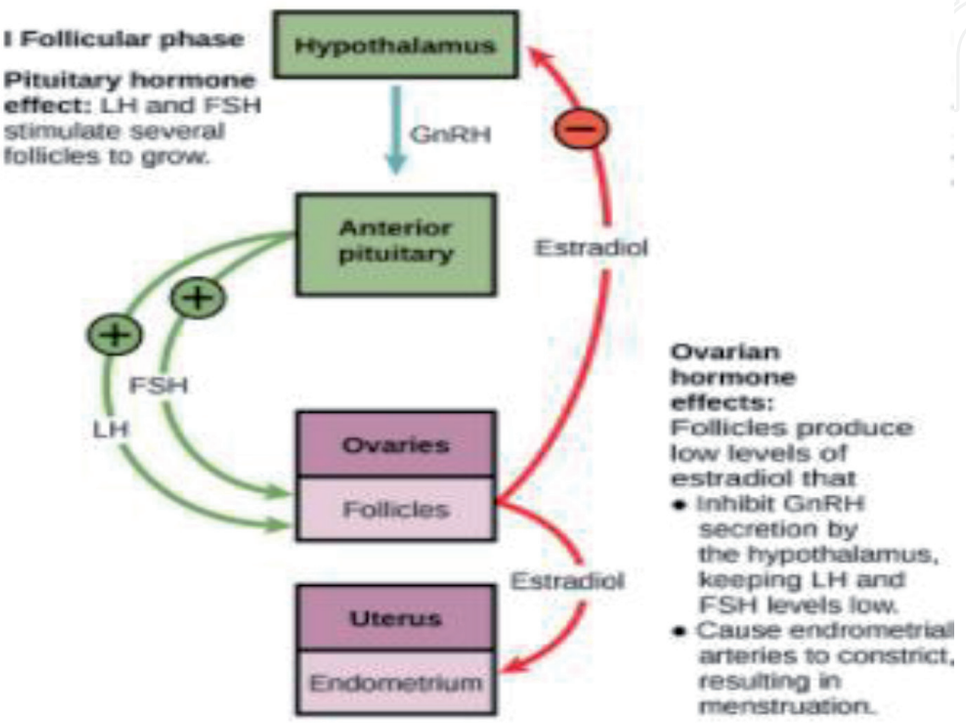


Figure 3.
The follicular phase [5].

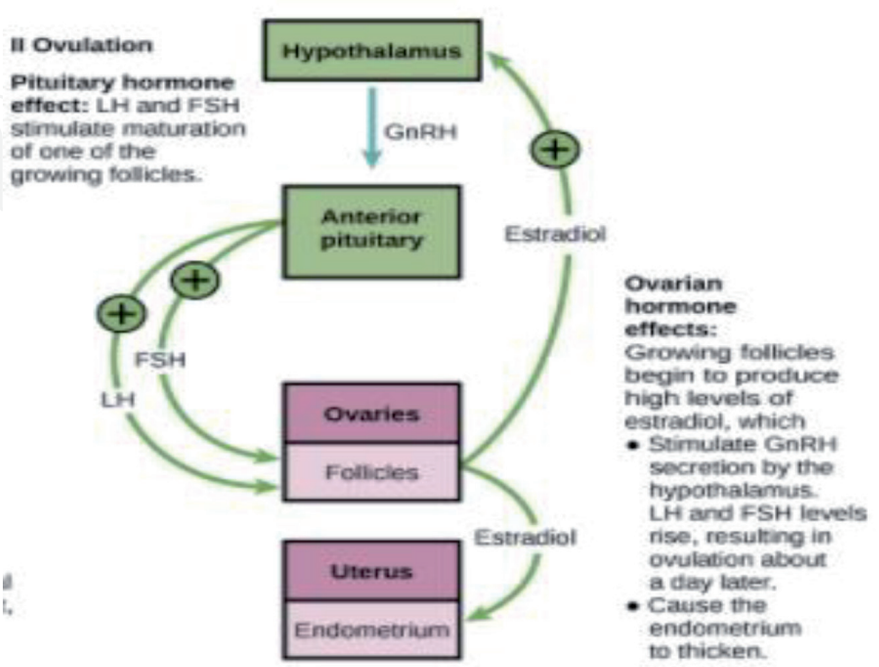


Figure 4.
The ovulation phase [5].

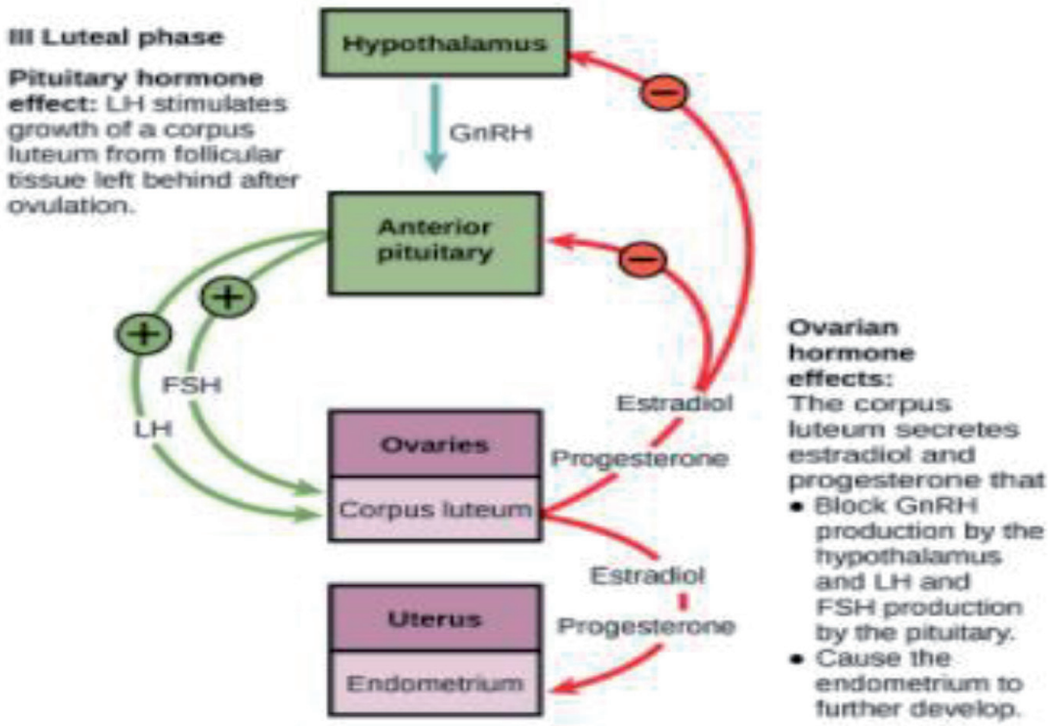


Figure 5.
The luteal phase [5].

maturation a follicle and thickens the endometrial lining. At this time, only 17-beta-estradiol (E2) provides positive feedback for FSH and LH production. A critical level of 17-beta-estradiol must be reached, at least 200 picograms per milliliter of plasma, to cause this positive feedback. The high levels of FSH and LH present during this time is called the LH surge [5]. The release of LH matures the ovum much further and weakens the wall of the follicle in the ovary, thus causing the fully developed follicle to release its secondary oocyte, in a process known as ovulation. After being released from the ovary, the ovum, also called egg, is swept into the fallopian tube.

The changes to the cervix which was initiated during the follicular phase is even further increased in ovulation phase allowing for increased, waterier cervical mucus in order to better accommodate the possible sperm. The levels of 17-beta-estradiol fall at the end of ovulation [1, 5, 6].

Luteal or Secretory phase: The luteal phase follows ovulation. It is characterized by the development of corpus luteum, secretion of progesterone and the formation of thick mucus which blocks the cervix. Blocking of the cervix is in anticipation that implantation has occurred [5]. Luteal phase always occurs from day 14 to day 28 of the cycle (See **Figure 1**). Progesterone stimulated by LH is the dominant hormone during this phase to prepare the corpus luteum and the endometrium for possible implantation of the fertilized ovum. As the luteal phase comes to an end, progesterone will provide negative feedback to the anterior pituitary to decrease FSH and LH levels and subsequently, the 17-beta-estradiol (E2) and progesterone levels [1, 5, 6].

Therefore, at the end of luteal phase, in the absence of implantation (pregnancy), when the level of progesterone drops, menses or menstruation occurs [1]. See **Figure 2**.

3. Clinical significance of physiology of normal uterine bleeding

A normal woman has an average of 450 menses throughout her lifetime. It is therefore, very important to fully understand the menstrual cycle and its physiology

as various complications may occur later in life for a woman [8]. The knowledge of this forms the cornerstone of making appropriate diagnosis and investigation [9].

Menstruation begins at puberty, usually between 10 to 16 years of age of a normal girl child. It ends at menopause, corresponding to average age of 45 to 55 years of a normal adult female [1].

Ordinarily, the typical volume of blood lost during menstruation is approximately 30 milliliters (mL). Any amount of blood lost during menstruation which is greater than 80 mL is considered abnormal [4].

The clinician needs to know all these in order to make appropriate diagnosis and investigation. Anything sort of this could result in gross errors.

4. Bleeding in fibroids

Fibroids are growths of muscle and fibrous tissue in or on the wall of the uterus.

They range in size from seedlings which are undetectable by human eye, to bulky masses that can disfigure or enlarge the uterus. One can have a single fibroid or multiple fibroids (See **Figure 6**) [10].

4.1 Normal versus abnormal bleeding

It is usually very difficult to tell between what is normal and what is abnormal when it comes to menstruation. This is because of the huge variation in women to the point that what is normal for one might be abnormal for another. Heavy menstrual flow is highly subjective.

In addition to the above, there are many factors that influence length, heaviness, and frequency of a woman's menstrual flow. Thus, paying close attention to one's monthly period and observing the trend becomes paramount to detecting whether or not one has abnormal or normal menstrual flow. This observance might need to have been done over a significant period of time [11].

Vaginal bleeding is considered to be abnormal if it occurs between a woman's menstrual cycles, in situations where flow is significantly heavier than normal for a particular individual or when it occurs after menopause.

4.1.1 Normal bleeding

Bleeding in normal period typically lasts between 3 and 8 days, usually with a heavier menstrual flow for the first two days. The flow gets increasingly lighter as

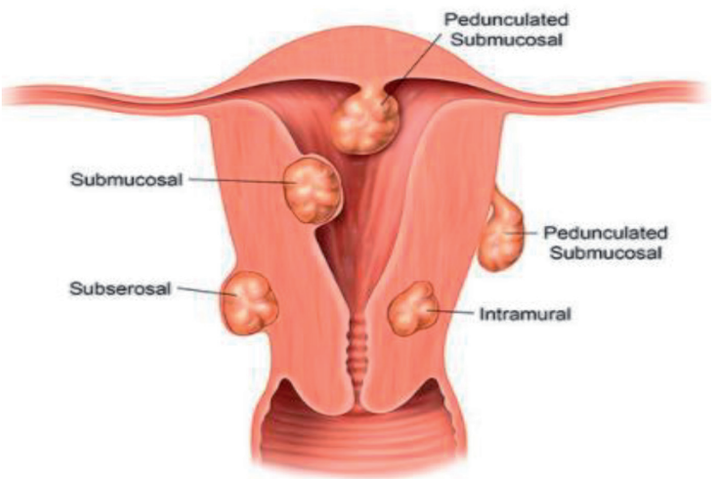


Figure 6.
Different locations of fibroids [10].

the number of days progress. Women with normal periods may have limited spotting, cramps that ache and bloating that goes away once the period is over.

4.1.2 Abnormal periods or fibroids bleeding

On another hand, abnormal bleeding, such as those bleedings occurring in fibroids and in heavy periods, usually lasts more than 10 days per month. Fibroid symptom involves persistent bleeding between menstrual cycles. This is to the point that can severely affect one's quality of life [11].

Abnormal bleeding can be considered missing 3 or more periods in a row, or periods which occur less than 21 days or more than 35 days apart from each other. Another sign of an abnormal period is bleeding through multiple pads and tampons in a short amount of time [10, 11].

4.2 The cause of heavy bleeding in fibroids

The cause of heavy bleeding in fibroid is not well understood. Since fibroids are connected to your uterine lining, the fibroids can exert pressure against the uterine wall and cause the endometrial tissue to bleed more than normal [11]. See **Figure 6.**

During menstrual period, the uterine lining sheds off and the uterus has two basic mechanisms to stop itself from bleeding. The first mechanism is through the normal blood-clotting working throughout the body by forming plugs within the blood vessels. Secondly, since the uterus is a muscle, it also has the ability to contract the bleeding vessels of the uterus, thus stopping the bleeding. The contractions are associated with menstrual cramps.

However, it is believed that fibroids interfere with adequate and proper contraction of the uterus. In this way, it does not stop menstrual bleeding adequately. Additionally, fibroids produce growth factors (proteins) that stimulate relaxation of the uterine blood vessels and thus causing more blood in the uterine cavity, which leads to heavier periods [11].

4.3 Treatment of abnormal bleeding and fibroids bleeding

The treatment of abnormal bleeding depend on; the cause, patient age, severity of bleeding and whether one wants to have children or not [12].

Otherwise, the common medical treatment options are;

1. Use of birth control pills

2. Hormone injections or a hormone-releasing IUD (intra-uterine device)

3. Surgery to control bleeding or to remove growths, such as fibroids, that are causing the bleeding. Surgical options available include endometrial ablation, endometrial polyp removal, myomectomy or even hysterectomy

The two medical treatments for heavy menstrual bleeding have been effective enough. First, levonorgestrel intra-uterine system was FDA approved for the treatment of heavy menstrual bleeding in 2009. It is highly effective for decreasing menstrual bleeding, treating anemia and improving the overall quality of life. Secondly, tranexamic acid, also FDA approved for heavy menstrual bleeding in 2009, reduces menstrual blood loss in 40% of women and improves quality of life. Moreover, in women with fibroids, tranexamic acid has been shown to decrease heavy menstrual bleeding and cause necrosis of the fibroids, especially larger fibroids [13].

5. Conclusion

Research on bleeding in fibroids is still far from over. Much more is still wanting.

Uterine fibroids are common debilitating problems for many women. Almost 60% of women with fibroids report that symptoms affect their quality of life and impede their physical activity. Again, 24% of them report that fibroid symptoms prevent them from reaching their full potential at work. Heavy menstrual bleeding, which is the most common symptom of uterine fibroids, affects approximately 1.4 million women per year.

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Conflict of interest

The author declares no conflict of interest.

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