



#### **Review Article**

# Amenorrhea-An abnormal cessation of normal menstrual cycle

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# **Abstract**

Amenorrhea is the absence or abnormal cessation of menstrual cycles in a woman of reproductive age. Prolonged cessation of menstrual cycles might results in complications such as infertility, psychosocial developmental delays, Osteoporosis, fractures etc. Better understanding of physiology of menstruation is essential to understand the various causes of primary and secondary amenorrhea. Any disruption or functional abnormality in the hypothalamic-pituitaryovarian axis can result in abnormal menstruation or amenorrhea. Therefore it is crucial to identify this menstrual distress in women at early age to minimize the risks of reproductive dysfunction in premenstrual and postmenstrual conditions.

# Introduction

The female menstrual cycle usually comprises of 28-30 days per cycle which contains two phases, the secretory phase and the proliferative phase [1]. At the termination of the cycle, the inner uterine layer starts shedding off which results in menstruation in females [2]. However in some case the absence of menstruation for two months or more in reproductively active female results in amenorrhea [3]. The term amenorrhea is defined as a disorder referred to the adolescent girl and women's who are not having normal menstrual cycle [4]. Menstrual cycle is a natural process that only ceases naturally during breastfeeding, pregnancy and menopause [5]. But intake of hormones and birth control results in amenorrhea in some women which is considered abnormal and is associated with various diseases such as estrogen deficient amenorrhea [6]. Estrogen deficient amenorrhea is a condition in which risks of having fractures is increased along with reduced level of bone minerals [7]. On the other hand estrogen replete amenorrhea leads to long term endometrial carcinoma and short-term uterine bleeding [8]. Another amenorrhea associated health issue is reported as hypothalamic pituitary-ovarian axis dysfunction among women's and young girl caused by physical exercises, anorexia, and stress [9]. In addition, Ovarian failures occurs due to hypergonadotropic amenorrhea [10].

# Consequences of amenorrhea

The following are some short/long term consequences of amenorrhea that are reported in females such as pelvic

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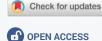
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pain, decreased bone density, hair loss, excessive facial/body hair, infertility, nipple discharge, headache, vaginal dryness, infertility, increased muscle size, decreased sex drive, acne and vision problems [11-14].

# Types of amenorrhea

Primarily amenorrhea is classified into two types' primary amenorrhea and secondary amenorrhea depending on its occurrence before and after the first-time menstruation [15].

a. Primary amenorrhea: Primary amenorrhea is an uncommon disorder or condition in which long-lasting absence of menstruation occurs [16]. Approximately 1% - 2% of women suffers from primary amenorrhea [17].

# Causes of primary amenorrhea

There are many causes of primary amenorrhea some of which are as follows:

a. End organ disorders: It includes abnormalities of chromosomes such as turner syndrome which causes gonadal dysgenesis [18] or the absence of breast bud by the age of 13 to 14 years indicates estradiol deficiency resulting in ovarian failure [19].



- **b. Outflow tract obstruction:** It includes, imperforated hymen, testicular feminization, transverse vaginal septum and atresia [20].
- **c. Central regulatory disorders:** Disorders such as pituitary disorders, hypothalamic disorders, pituitary tumours, androgen insensitivity, congenital gonadotropin-releasing hormone (GnRH) deficiency and Kallmann syndrome are some examples of central regulatory disorders that causes primary amenorrhea [21,22].
- **d. Secondary amenorrhea:** Occurrence of secondary amenorrhea in women's is about 3% to 5% [23]. Absence of menstruation cycle for 2 to 3 consecutive fertility cycles in women or if the cessation is for 6 or more months results in secondary amenorrhea [24].

# Causes of secondary amenorrhea

There are many causes of secondary amenorrhea such as pregnancy, low or normal FSH, anorexia, nonspecific hypothalamic, chronic anovulation, hypothyroidism, cushing syndrome, abnormalities, asherman syndrome, ovarian dysfunction etc [25,26].

#### Etiology of amenorrhea

The following factors are responsible for causing amenorrhea:

- **a. Natural factors:** The natural factors that causes amenorrhea includes breastfeeding, age, menopause and pregnancies [27].
- **b. Role of medicine:** Intake of high medicinal drugs are responsible for disturbing menses and causing amenorrhea such drugs includes anti-allergies, injectable contraceptives, anti-BP drug, anti-psychotics, birth control pills, anti-depressants etc [28].
- **c. Nutritional deficiency:** Nutritional deficiency causes hypothalamic disorders leading to severe menstrual issues [29].
- d. Behavioral and lifestyle factors: Malnourished diet, weight issues, alcohol consumption, elevated intake of coffee, tea and smoking periodically effects the natural menstrual cycle n females [30,31].
- **e. Exercise:** Generally exercise-induced amenorrhea results from the suppression of GnRH leading to hypoestrogenism and delayed menstrual cycle [32].
- **f. Dietary factors:** High intake of fruits and vegetables delays the onset of menopause and prolongs the reproductive lifespan because of the presence of antioxidants in fruits and vegetables that counteracts the adverse effects of reactive oxygen species on the number and quality of ovarian follicles [33].

- **g. Hormonal imbalance:** Due to hormonal imbalance amenorrhea in women may result in serious consequences such as thyroid malfunction, polycystic ovary syndrome, tumor of pituitary gland sarcoids, premature menopause, premature ovarian failure, postpartum necrosis etc [34,35].
- **h. Female reproductive system:** Abnormalities like reproductive organ, birth defects, genital tract defects, ovary infections etc are also responsible for causing amenorrhea [36].
- i. Genetic defects: Genetic defects are also one of the factors that causes amenorrhea in women such as chromosomal abnormalities like Turner syndrome, sawyer syndrome, Fragile X syndrome and Kallmann syndrome [37,38].
- j. Less common causes: The unusual causes of amenorrhea includes autoimmune disorders, head injuries, over growth of tissue from placenta, and polyps, cancer, cushing syndrome, chronic disorders, AIDS, adrenal gland malfunction, fibroids and chemotherapy [39,40].

# **Epidemiology of amenorrhea**

Amenorrhea is not life-threatening, but the lack of menstrual cycle has been associated with high risk of hip and wrist fractures [41]. In the, amenorrhea affects about 1 % of women [42]. Recent studies indicated that childhood obesity may contribute to the early onset of amenorrhea [43].

#### **Treatment of amenorrhea**

- a. The following are some treatments recommended for amenorrhea:Amenorrhea could be treated using either medicines that reduces abnormal hormone levels [44] or by means of tumour surgeries to remove structural defects in organs that are involved in menstrual cycle [45].
- b. In addition estrogen therapy and mineral supplements could be helpful in reducing amenorrhea associated health risks [46].
- c. Besides factors like stress, eating disorders etc requires change in patient's attitude and diet [47]. In addition to that a woman is advised to keep a track of their menstrual cycles and should often visit their gynecologists for a regular checkup [48].
- d. In case of athletes, women are advised to reduce the intensity of their physical activities and intake of supplementary hormones which causes heavy prolonged bleeding and depression [49].

# Conclusion

Thus it is concluded that amenorrhea is a menstrual associated problem affecting women all over the world.



Therefore it is important to identify those factors responsible for causing primary/secondary amenorrhea in adolescent girls and women for the sake of their healthy reproductive functioning.

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