

Review Article

Amenorrhea-An abnormal cessation of normal menstrual cycle

Nida Tabassum Khan* and Namra Jameel

Department of Biotechnology, Faculty of Life Sciences and Informatics, Balochistan University of Information Technology Engineering and Management Sciences, (BUITEMS), Quetta, Pakistan

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-pituitary-ovarian 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

More Information

***Address for Correspondence:** Nida Tabassum Khan, Department of Biotechnology, Faculty of Life Sciences and Informatics, Balochistan University of Information Technology Engineering and Management Sciences, (BUITEMS), Quetta, Pakistan, Tel: 03368164903; Email: nidadabassmkhan@yahoo.com; nidadabassumkhan@yahoo.com

Submitted: 16 March 2020

Approved: 08 April 2020

Published: 09 April 2020

How to cite this article: Khan NT, Jameel N. Amenorrhea-An abnormal cessation of normal menstrual cycle. Clin J Obstet Gynecol. 2020; 3: 033-036.

DOI: 10.29328/journal.cjog.1001046

Copyright: © 2020 Khan NT, et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Keywords: Secondary amenorrhea; Gonadal dysgenesis; Hypothalamic disorders; Infertility; Estrogen deficient



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.

References

- Treloar AE, Boynton RE, Behn BG, Brown BW. Variation of the human menstrual cycle through reproductive life. *Int J Fertil*. 1967; 12: 77-126. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/5419031): <https://www.ncbi.nlm.nih.gov/pubmed/5419031>
- Vollman RF. The menstrual cycle. *Major Probl Obstet Gynecol*. 1977; 7: 1-193. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/836520): <https://www.ncbi.nlm.nih.gov/pubmed/836520>
- Master-Hunter T, Heiman DL. Amenorrhea: evaluation and treatment. *Am Family Physician*. 2006; 73: 1374-1382.
- Practice Committee of the American Society for Reproductive Medicine. Current evaluation of amenorrhea. *Fertil Steril*. 2004; 82: 33-39. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/19007635): <https://www.ncbi.nlm.nih.gov/pubmed/19007635>
- Heiman DL. Amenorrhea. *Prim Care*. 2009; 36: 1-17. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/19231599): <https://www.ncbi.nlm.nih.gov/pubmed/19231599>
- Grinspoon S, Miller K, Coyle C, Krempin J, Armstrong C, et al. Severity of osteopenia in estrogen-deficient women with anorexia nervosa and hypothalamic amenorrhea. *J Clin Endocrinol Metab*. 1999; 84: 2049-2055. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/10372709): <https://www.ncbi.nlm.nih.gov/pubmed/10372709>
- Gordon CM. Functional hypothalamic amenorrhea. *N Eng J Med*. 2010; 363: 365-371.
- Golden NH, Carlson JL. The pathophysiology of amenorrhea in the adolescent. *Ann N Y Acad Sci*. 2008; 1135: 163-178. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/18574222): <https://www.ncbi.nlm.nih.gov/pubmed/18574222>
- Rothman MS, Wierman ME. Female hypogonadism: evaluation of the hypothalamic-pituitary-ovarian axis. *Pituitary*. 2008; 11: 163-169. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/18404388): <https://www.ncbi.nlm.nih.gov/pubmed/18404388>
- Rebar RW. Hypergonadotropic amenorrhea and premature ovarian failure: a review. *J Reprod Med*. 1982; 27: 179-186. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/6808131): <https://www.ncbi.nlm.nih.gov/pubmed/6808131>
- Benson JE, Engelbert-Fenton KA, Eisenman PA. Nutritional aspects of amenorrhea in the female athlete triad. *Int J Sport Nutr*. 1996; 6: 134-145. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/8744786): <https://www.ncbi.nlm.nih.gov/pubmed/8744786>
- Mclver B, Romanski SA, Nippoldt TB. Evaluation and management of amenorrhea. *Mayo Clin Proc*. 1997; 72: 1161-1169. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/9413300): <https://www.ncbi.nlm.nih.gov/pubmed/9413300>
- Hirschberg AL, Hagenfeldt K. Athletic amenorrhea and its consequences. Hard physical training at an early age can cause serious bone damage. *Lakartidningen*. 1998; 95: 5765-5770. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/9889498): <https://www.ncbi.nlm.nih.gov/pubmed/9889498>
- Meczekalski B, Katulski K, Czyzyk A, Podfigurna-Stopa A, Maciejewska-Jeske M. Functional hypothalamic amenorrhea and its influence on women's health. *J Endocrinol Invest*. 2014; 37: 1049-1056. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/25201001): <https://www.ncbi.nlm.nih.gov/pubmed/25201001>
- Rebar RW, Connolly HV. Clinical features of young women with hypergonadotropic amenorrhea. *Fertil Steril*. 1990; 53: 804-810. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/2110072): <https://www.ncbi.nlm.nih.gov/pubmed/2110072>
- Master-Hunter T, Heiman DL. Amenorrhea: evaluation and treatment. *Am Fam Physician*. 2006; 73: 1374-1382. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/16669559): <https://www.ncbi.nlm.nih.gov/pubmed/16669559>
- Timmreck LS, Reindollar RH. Contemporary issues in primary amenorrhea. *Obstet Gynecol Clin North Am*. 2003; 30: 287-302. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/12836721): <https://www.ncbi.nlm.nih.gov/pubmed/12836721>
- Chae HD, Kang EH, Chu HS, Kim JH, Kang BM, et al. Clinical characteristics of amenorrhea according to the etiological classification. *Korean J Obstet Gynecol*. 1999; 42: 975-980.
- Child T. Investigation and treatment of primary amenorrhoea. *Obstetrics, Gynaecology & Reproductive Medicine*. 2011; 21: 31-35.
- Lardenoije C, Aardenburg R, Mertens H. Imperforate hymen: a cause of abdominal pain in female adolescents. *BMJ Case Rep*. 2009; bcr0820080722. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/21686660): <https://www.ncbi.nlm.nih.gov/pubmed/21686660>
- Liu JH, Patel B, Collins G. Central causes of amenorrhea. In *Endotext [Internet]*. 2016. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/25905176): <https://www.ncbi.nlm.nih.gov/pubmed/25905176>
- Pletcher JR, Slap GB. Menstrual disorders: amenorrhea. *Pediatr Clin North Am*. 1999; 46: 505-518. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/10384804): <https://www.ncbi.nlm.nih.gov/pubmed/10384804>
- Petterson F, Fries H, Nillius SJ. Epidemiology of secondary amenorrhea: I. Incidence and prevalence rates. *Am J Obstet Gynecol*. 1973; 117: 80-86. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/4722382): <https://www.ncbi.nlm.nih.gov/pubmed/4722382>
- Drew FL. The epidemiology of secondary amenorrhea. *J Chronic Dis*. 1961; 14: 396-407. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/13887810): <https://www.ncbi.nlm.nih.gov/pubmed/13887810>
- Koninckx PR, Brosens IA. The "gonadotropin-resistant ovary" syndrome as a cause of secondary amenorrhea and infertility. *Fertil Steril*. 1977; 28: 926-931. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/892043): <https://www.ncbi.nlm.nih.gov/pubmed/892043>
- McGee C. Secondary amenorrhea leading to osteoporosis: incidence and prevention. *Nurse Pract*. 1997; 22: 38-41. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/9172234): <https://www.ncbi.nlm.nih.gov/pubmed/9172234>
- Howie PW. Breastfeeding: a natural method for child spacing. *Am J Obstet Gynecol*. 1991; 165: 1990-1991. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/1755455): <https://www.ncbi.nlm.nih.gov/pubmed/1755455>
- Tanmahasamut P, Rattanachaiyanont M, Dangrat C, Indhavivadhana S, Angsuwattana S, et al. Causes of primary amenorrhea: a report of 295 cases in Thailand. *J Obstet Gynaecol Res*. 2012; 38: 297-301. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/22070792): <https://www.ncbi.nlm.nih.gov/pubmed/22070792>
- Warren MP, Fried JL. Hypothalamic amenorrhea: the effects of environmental stresses on the reproductive system: a central effect of the central nervous system. *Endocrinol Metab Clin North Am*. 2001; 30: 611-629. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/11571933): <https://www.ncbi.nlm.nih.gov/pubmed/11571933>
- Benson JE, Engelbert-Fenton KA, Eisenman PA. Nutritional aspects of amenorrhea in the female athlete triad. *Int J Sport Nutr*. 1996; 6: 134-145. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/8744786): <https://www.ncbi.nlm.nih.gov/pubmed/8744786>
- Hally SS. Nutrition in reproductive health. *J Nurse Midwifery*. 1998; 43: 459-470. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/9871379): <https://www.ncbi.nlm.nih.gov/pubmed/9871379>
- Schwartz B, Cumming DC, Riordan E, Selye M, Yen SS, et al. Exercise-associated amenorrhea: a distinct entity?. *Am J Obstet Gynecol*. 1981; 141: 662-670. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/7315895): <https://www.ncbi.nlm.nih.gov/pubmed/7315895>
- De Souza MJ, Williams NI. Beyond hypoestrogenism in amenorrheic athletes: energy deficiency as a contributing factor for bone loss. *Curr Sports Med Rep*. 2005; 4: 38-44. [PubMed](https://www.ncbi.nlm.nih.gov/pubmed/15659278): <https://www.ncbi.nlm.nih.gov/pubmed/15659278>



34. Rashid BM, Mahmoud TJ, Nore BF. Hormonal study of primary infertile women. *J Zankoy Sulaimani-Part A*. 2013; 15: 2.
35. MacGregor TN. Amenorrhoea: Aetiology and Treatment. *Br Med J*. 1938; 1: 717.-722.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20781357>
36. Yen SS. Female hypogonadotropic hypogonadism: hypothalamic amenorrhea syndrome. *Endocrinol Metab Clin North Am*. 1993; 22: 29-58.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/8449187>
37. Caronia LM, Martin C, Welt CK, Sykiotis GP, Quinton R, et al. A genetic basis for functional hypothalamic amenorrhea. *N Engl J Med*. 2011; 364: 215-225.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21247312>
38. Seminara SB, Crowley Jr WF. Perspective: the importance of genetic defects in humans in elucidating the complexities of the hypothalamic-pituitary-gonadal axis. *Endocrinology*. 2001; 142: 2173-2177.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11356659>
39. Wilson GR, Haddad JE, Haddad CJ. Amenorrhea common causes and evaluation. *Compr Ther*. 2005; 31: 270-278.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16407607>
40. Reindollar RH, Novak M, Tho SP, McDonough PG. Adult-onset amenorrhea: a study of 262 patients. *Am J Obstet Gynecol*. 1986; 155: 531-541.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/3529965>
41. Bachmann GA, Kemmann E. Prevalence of oligomenorrhea and amenorrhea in a college population. *Am J Obstet Gynecol*. 1982; 144: 98-102.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/7114117>
42. Harlow SD, Campbell OM. Epidemiology of menstrual disorders in developing countries: a systematic review. *BJOG*. 2004; 111: 6-16.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14687045>
43. Fries H, Nillius SJ, Pettersson F. Epidemiology of secondary amenorrhea: II. A retrospective evaluation of etiology with special regard to psychogenic factors and weight loss. *Am J Obstet Gynecol*. 1974; 118: 473-479.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/4812568>
44. Zondek B. Simplified hormonal treatment of amenorrhea. *J Am Med Assoc*. 1942; 118: 705-707.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12259270>
45. Warren MP, Hagey AR. The genetics, diagnosis and treatment of amenorrhea. *Minerva Ginecol*. 2004; 56: 437-455.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15531861>
46. Golden NH, Lanzkowsky L, Schebendach J, Palestro CJ, Jacobson MS, et al. The effect of estrogen-progestin treatment on bone mineral density in anorexia nervosa. *J Pediatr Adolesc Gynecol*. 2002; 15: 135-143.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12106749>
47. Chen YT, Tenforde AS, Fredericson M. Update on stress fractures in female athletes: epidemiology, treatment, and prevention. *Curr Rev Musculoskelet Med*. 2013; 6: 173-181.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23536179>
48. Dueck CA, Matt KS, Manore MM, Skinner JS. Treatment of athletic amenorrhea with a diet and training intervention program. *Int J Sport Nutr*. 1996; 6: 24-40.
PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/8653102>
49. Bennell K, Brukner P. Preventing and managing stress fractures in athletes. *Physical Therapy in Sport*. 2005; 6: 171-180.