

DOI: <https://dx.doi.org/10.18203/2320-1770.ijrcog20263990>

Original Research Article

Analysis of secondary amenorrhea in reproductive age group: a prospective observational study

Himani Gupta*, Swathi P. S., Sangeeta Kamra

Department of Obstetrics and Gynecology, Jawaharlal Nehru Hospital and Research Centre, Bhilai, Chhattisgarh, India

Received: 02 September 2026

Revised: 08 October 2026

Accepted: 09 October 2026

*Correspondence:

Dr. Himani Gupta,

E-mail: himanigupta270678@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Secondary amenorrhea is a clinically important and has diverse hypothalamic, pituitary, ovarian and endocrine causes. Identification of the underlying cause is essential as persistent anovulation may affect fertility and long-term health. The topic was undertaken due to the scarcity of data from central India. Objective was to identify the etiology and review the differential diagnosis of secondary amenorrhea among women of reproductive age.

Methods: A prospective observational study was conducted in the department of obstetrics and gynecology, JLNHRC, Bhilai, Chhattisgarh, over 18 months. 72 women of reproductive age having secondary amenorrhea were enrolled. Patients with pregnancy, lactation, menopause or using Mirena or depot medroxyprogesterone acetate were excluded. Detailed clinical evaluation, UPT, CBC, serum TSH, serum prolactin, pelvic ultrasound and progesterone challenge test were performed. Etiological patterns and associations with BMI, lifestyle, stress and dietary habits were analysed.

Results: The participants were between 16-35 years. 44 (61.1%) were unmarried. Among 28 married women, 17 had associated infertility. 44 (61.1%) were overweight or obese. PCOS was identified in 21 (29.2%), hypothyroidism in 16 (22.2%) and hyperprolactinemia in 6 (8.3%) women. In 33 (45.8%) no specific cause was identified by available preliminary evaluation and these were classified as probable functional hypothalamic amenorrhea (FHA). Among women with PCOS, BMI was significantly associated with diagnosis ($p < 0.001$). Probable FHA showed significant associations with lifestyle ($p = 0.004$), dietary habits ($p = 0.0026$), BMI ($p = 0.015$) and stress ($p = 0.028$).

Conclusions: Secondary amenorrhea has a heterogeneous etiology. A structured clinical assessment with basic laboratory investigations and pelvic ultrasonography can identify a substantial proportion of causes without immediately resorting to extensive hormonal testing. Obesity, lifestyle, dietary habits and psychological stress are modifiable, while persistent or atypical cases require further endocrine and structural evaluation.

Keywords: Functional hypothalamic amenorrhea, Hyperprolactinemia, Hypothyroidism, Infertility, Polycystic ovary syndrome, Secondary amenorrhea

INTRODUCTION

Menstrual regularity is an important marker of reproductive and general health. Normal menstruation requires coordinated function of the hypothalamic-pituitary-ovarian axis, a responsive endometrium and an intact genital outflow tract. Disruption at any level may result in amenorrhea. Secondary amenorrhea is defined as absence of menstruation for at least three consecutive

cycles in a woman who previously menstruated regularly or for approximately six months in women with previously irregular cycles.^{1,2} While investigating secondary amenorrhoea, physiological causes such as pregnancy, lactation and menopause must first be excluded, after which the differential diagnosis includes hypothalamic or pituitary dysfunction, PCOS, thyroid dysfunction, hyperprolactinaemia, primary ovarian insufficiency and uterine or outflow tract disorders.^{1,3}

Functional hypothalamic amenorrhea (FHA) is a form of hypothalamic hypogonadism associated with disturbances in energy balance, stress, excessive exercise and other behavioural or psychosocial factors. It is a diagnosis of exclusion and may coexist with changes in body weight or dietary practices.^{4,5} PCOS is another important cause of chronic anovulation and amenorrhea and is frequently associated with overweight, obesity and insulin resistance.⁶ Thyroid dysfunction and hyperprolactinaemia may also interfere with the hypothalamic-pituitary-ovarian axis and produce menstrual dysfunction.⁷⁻⁹

A carefully obtained history, examination and a focused first-line investigation panel can often help in diagnosis.^{1,3} This approach is particularly relevant in resource-limited settings. There are very few studies describing the etiology of secondary amenorrhea from central India. Hence, the present study was therefore undertaken to analyse the causes and associated factors of secondary amenorrhea among reproductive-age women attending a tertiary-care hospital in Bhilai, Chhattisgarh.

METHODS

Study design and setting

This prospective observational study was conducted in the department of obstetrics and gynecology, Jawaharlal Nehru Hospital and Research Centre, Bhilai, Chhattisgarh, over 18 months from 5 June 2022 to 4 December 2023.

Study population

Women of reproductive age attending the gynecology outpatient department with secondary amenorrhea.

Sample size

72 women with history of secondary amenorrhoea were included in the study.

Inclusion criteria

Women with previously established menstruation who had absence of menses for three or more consecutive cycles, or for six months or longer and who consented to participate.

Exclusion criteria

Pregnant, lactating or menopausal women or those using a levonorgestrel intrauterine system (Mirena) or depot medroxyprogesterone acetate.

Assessment

A detailed history was obtained regarding age, marital status, menstrual pattern and duration of amenorrhea, obstetric and infertility history, lifestyle, dietary habits, weight change, medication use, chronic illness, symptoms

of androgen excess and galactorrhoea. Height and weight were recorded and body mass index (BMI) was calculated. General, systemic and relevant pelvic examinations were performed; speculum and vaginal examinations were restricted to sexually active participants with appropriate consent.

Investigations

Pregnancy was excluded with a urine pregnancy test. The available first-line investigations included complete blood count, serum thyroid-stimulating hormone (TSH), serum prolactin and pelvic ultrasonography to assess the uterus, endometrial thickness and adnexa. A progesterone challenge test was performed to assess withdrawal bleeding. All participants in the study responded to the progesterone challenge test. Patients in whom no specific cause was identified by the preliminary evaluation were classified as having probable FHA. This terminology was deliberately used because definitive diagnosis of FHA generally requires exclusion of other endocrine and structural causes and may require gonadotropin and estradiol assessment and, in selected patients, pituitary imaging.^{4,5}

Statistical analysis

Data were summarised using numbers and percentages. Associations between probable etiological factors and clinical variables were assessed using appropriate statistical tests, and $p < 0.05$ considered as statistically significant. The analysis reported p values for associations between PCOS and BMI and between probable FHA and lifestyle, BMI, stress and dietary habits.

RESULTS

A total of 72 women with secondary amenorrhea were enrolled. Age ranged from 16 to 35 years. The two-thirds of participants were aged 21–30 years. 44 participants were unmarried. Out of the 28 married women, 17 had associated infertility; 12 primary and 5 secondary. This finding highlights the relevance of amenorrhea in fertility evaluation for women of reproductive age.

Of the 72, 28 women (38.9%) had normal BMI, 32 (44.4%) were overweight and 12 (16.7%) were obese. No participant was underweight. 43 women (59.7%) reported a sedentary lifestyle, 17 (23.6%) had mild physical activity and 12 (16.7%) had moderate physical activity. Most patients presented with amenorrhea of 3–6 months duration (88.9%) and (61.1%) had previous history of regular menstrual cycles.

Pelvic ultrasonography showed significant abnormalities in 22 women. Polycystic ovarian morphology was reported in 19, functional ovarian cyst in 2 and bulky uterus with features of adenomyosis in 1 patient.

Table 1: Baseline characteristics of women with secondary amenorrhea (n=72).

Characteristics	Category	N (%)
Age (years)	Menarche-20	16 (22.2)
	21-25	28 (38.9)
	26-30	20 (27.8)
	31-35	8 (11.1)
BMI	Normal	28 (38.9)
	Overweight	32 (44.4)
	Obese	12 (16.7)
Lifestyle	Sedentary	43 (59.7)
	Mild physical activity	17 (23.6)
	Moderate physical activity	12 (16.7)
Duration of amenorrhea	3-6 months	64 (88.9)
	>6 months	8 (11.1)
Previous menstrual cycles	Regular	44 (61.1)
	Irregular	28 (38.9)
Marital status	Unmarried	44 (61.1)
	Married	28 (38.9)
Pelvic ultrasonography	Normal	50 (69.4)
	PCOS morphology	19 (26.4)
	Other abnormalities*	3 (4.2)
Hemoglobin status	Normal	51 (70.8)
	Mild anemia	19 (26.4)
	Moderate anemia	2 (2.8)

*Includes functional ovarian cyst (n=2) and adenomyosis (n=1).

Table 2: Etiological distribution and overlapping causes of secondary amenorrhea (n=72).

Etiology	N	%
Single-factor etiologies		
PCOS	16	22.2
Hypothyroidism	10	13.9
Hyperprolactinemia	3	4.2
Moderate anemia	2	2.8
Ovarian cyst	1	1.4
Multiple-factor etiologies		
PCOS + hypothyroidism	3	4.2
Hypothyroidism + hyperprolactinemia	2	2.8
PCOS + hyperprolactinemia	1	1.4
PCOS + hypothyroidism + ovarian cyst	1	1.4
Functional hypothalamic amenorrhea	33	45.8
Total	72	100

All patients responded to the progesterone challenge test, thereby excluding anatomical causes of secondary amenorrhea. Functional hypothalamic amenorrhea (FHA) was the most common etiology, accounting for 45.8% (33) of cases. Among the endocrine causes, PCOS was the most frequent diagnosis, identified in 29.1% (21) of patients, followed by hypothyroidism (22.2%, 16) and hyperprolactinemia (8.2%, 6).

Of the 21 patients with PCOS, 76.2% had isolated PCOS, while the remainder had associated hypothyroidism or

hyperprolactinemia. Most PCOS patients fulfilled the Rotterdam ultrasonographic criteria, and approximately half demonstrated clinical features of hyperandrogenism. Among the 16 hypothyroid patients, 62.5% had isolated hypothyroidism, while 25% had associated PCOS and 12.5% had concomitant hyperprolactinemia. Hyperprolactinemia was identified in six patients, of whom 50% had isolated hyperprolactinemia, while the remainder had associated hypothyroidism or PCOS.

Analysis of associated factors revealed a significant relationship between PCOS and obesity ($p<0.001$), with 83.3% of obese women diagnosed with PCOS. No significant association was observed between PCOS and lifestyle pattern or dietary habits. In contrast, FHA showed significant associations with normal BMI ($p=0.015$), physical activity level ($p=0.004$), stress ($p=0.028$), and junk-food consumption ($p=0.0026$). The prevalence of FHA was highest among women with moderate physical activity (75%), followed by mild physical activity (64.7%), and was more common among those reporting stress and junk-food consumption.

Overall, the findings indicate that FHA, PCOS, and hypothyroidism were the predominant causes of secondary amenorrhea, with obesity being strongly associated with PCOS, whereas lifestyle-related factors and psychosocial stress were more closely associated with FHA.

Table 3: Detailed analysis of major endocrine causes of secondary amenorrhea.

Variables	Category	N	%
PCOS (n=21)	Amenorrhea + USG PCOS	10	47.6
	Amenorrhea + USG PCOS + Hyperandrogenism	9	42.9
	Amenorrhea + Clinical Hyperandrogenism	2	9.5
Hyperandrogenic features (n=11)	Hirsutism	5	45.5
	Acne	3	27.3
	Hirsutism + Acne + Acanthosis	2	18.2
	Hirsutism + Acne	1	9.1
Hypothyroidism (n=16)	Isolated hypothyroidism	10	62.5
	Associated with PCOS	4	25.0
	Associated with Hyperprolactinemia	2	12.5
TSH Status (n=16)	Newly diagnosed	9	56.2
	Previously diagnosed, uncontrolled	3	18.8
	Previously diagnosed, controlled	4	25.0
Hyperprolactinemia (n=6)	Isolated	3	50.0
	Associated with hypothyroidism	2	33.3
	Associated with PCOS	1	16.7

Table 4: Association of PCOS with BMI, lifestyle and dietary habits (n=72).

Variables	Category	Total Patients N	PCOS Cases N (%)	P value
BMI	Normal	28	3 (10.7)	<0.001*
	Overweight	32	8 (25.0)	
	Obese	12	10 (83.3)	
Lifestyle	Sedentary	43	16 (37.2)	0.12
	Mild physical activity	17	4 (23.5)	
	Moderate physical activity	12	1 (8.3)	
Dietary habits	Junk food consumption present	41	11 (28.6)	0.61
	Junk food consumption absent	31	10 (32.2)	

Table 5: Association of functional hypothalamic amenorrhea (FHA) with BMI, lifestyle, stress and dietary habits (n=72).

Variables	Category	Total patients N	FHA Cases N (%)	P value
BMI	Normal BMI	28	18 (64.2)	0.015*
	Overweight	32	13 (40.6)	
	Obese	12	2 (16.6)	
Lifestyle	Sedentary	43	13 (30.2)	0.004†
	Mild physical activity	17	11 (64.7)	
	Moderate physical activity	12	9 (75.0)	
Stress	Present	42	22 (52.4)	0.028*
	Absent	30	11 (36.7)	
Dietary habits	Junk food consumption present	41	26 (63.4)	0.0026†
	Junk food consumption absent	31	7 (22.6)	

*Statistically highly significant. †Statistically highly significant.

DISCUSSION

The present study demonstrates that secondary amenorrhea in reproductive-age women is etiologically heterogeneous and that a focused clinical evaluation can identify important endocrine and functional patterns. The predominance of women aged 21-30 years is clinically relevant because this is the period when menstrual

regularity, fertility planning and metabolic health frequently intersect.

The most frequent category in this cohort was probable FHA, accounting for 45.8% of cases. This proportion is higher than the 20-35% range commonly reported for functional hypothalamic causes in broader descriptions of secondary amenorrhea.^{1,4} A recent specialist-centre study by Möro et al reported functional hypothalamic

hypogonadism as a major cause among patients referred for amenorrhea, while Kafeel et al reported functional secondary amenorrhea in approximately 39.7% of their study population.^{10,11} The higher proportion in the present study may reflect the referral profile and, importantly, the use of the term probable FHA for patients in whom a specific cause was not demonstrated by the available preliminary investigations.

The interpretation of probable FHA deserves caution. FHA is a diagnosis of exclusion, and definitive evaluation can require serum gonadotropins and estradiol, assessment of nutritional and psychological factors and, when indicated, pituitary imaging.^{4,5} In the present setting, complete hormonal profiling was not feasible for every participant. Nevertheless, the significant associations observed between probable FHA and lifestyle, dietary habits, stress and BMI support the clinical relevance of functional and behavioural factors. The results also suggest that counselling regarding nutrition, physical activity, weight management and stress should form part of the initial management of women with otherwise unexplained amenorrhea.

PCOS was the most frequent specific diagnosis, affecting 29.2% of participants. PCOS is a common endocrine disorder characterized by ovulatory dysfunction and hyperandrogenism, with polycystic ovarian morphology in some patients.^{12,13} The strong association between PCOS and BMI in this cohort ($p < 0.001$) is consistent with the well-recognised relationship between excess adiposity, insulin resistance and reproductive dysfunction. Lifestyle intervention is therefore clinically important, particularly for overweight and obese women with PCOS.¹²

Hypothyroidism was identified in 22.2% of participants. Thyroid dysfunction can alter reproductive function through effects on the hypothalamic-pituitary-ovarian axis and, in hypothyroidism, through changes in thyrotropin-releasing hormone and prolactin secretion.^{7,14} The prevalence in the present study was comparable to the 22% reported by Ajmani et al among women with menstrual disorders in a tertiary-care setting.¹⁴ The finding also reinforces the value of serum TSH as a relatively accessible first-line test in the evaluation of secondary amenorrhea.

Hyperprolactinaemia was present in 8.3% of women, close to the prevalence reported in other studies of menstrual disorders.^{8,9,15} Prolactin excess suppresses pulsatile gonadotropin-releasing hormone secretion and may cause hypogonadism and amenorrhea.¹⁵ The overlap with hypothyroidism observed in the present cohort is biologically plausible because severe primary hypothyroidism can increase thyrotropin-releasing hormone and contribute to hyperprolactinaemia.¹⁶

An important finding was the high proportion of women who were overweight or obese: 44.4% were overweight and 16.7% obese. This is relevant because both PCOS-

related anovulation and other forms of menstrual dysfunction can be associated with excess adiposity.^{12,17} The absence of underweight participants in this cohort suggests that the study population differed from classical FHA cohorts in which low energy availability and excessive exercise are prominent. This further supports the need to avoid assuming a single phenotype of functional amenorrhea.

The presence of infertility in 17 of 28 married women also underscores the reproductive implications of secondary amenorrhea. Amenorrhea frequently reflects anovulation, and restoration of normal endocrine function may improve fertility in selected patients. However, the present study did not include sufficient longitudinal follow-up to determine whether correction of the identified factors resulted in restoration of fertility. Therefore, the association should be regarded as clinically important rather than as a demonstrated outcome of the intervention.

The study has several strengths. It was prospective, included all eligible reproductive-age women presenting during the study period and systematically recorded clinical, lifestyle and basic laboratory variables. It also provides data from central India, where published studies specifically addressing the etiological profile of secondary amenorrhea are relatively limited. However, the study has limitations. The sample size was modest and derived from a single tertiary-care centre. The study population consisted predominantly of employees or spouses of employees of the associated steel plant, which may limit generalisability. Complete hormonal profiles, including FSH, LH and estradiol, were not available for all participants, and pituitary imaging was not routinely performed. Consequently, the category of probable FHA should not be interpreted as a definitive endocrine diagnosis. Long-term menstrual and fertility outcomes were also not assessed.

The findings support a pragmatic diagnostic approach: pregnancy should be excluded first, followed by careful history and examination and selected first-line investigations including TSH, prolactin and pelvic ultrasonography. Further hormonal testing and imaging should be reserved for persistent, recurrent, atypical or clinically suspicious cases, including those with virilisation, severe hyperandrogenism, galactorrhoea, evidence of ovarian insufficiency or failure to respond to initial management. This approach can reduce unnecessary investigations while maintaining appropriate vigilance for important endocrine and structural disease.

CONCLUSION

Secondary amenorrhea in reproductive-age women has multiple interacting causes. In this tertiary-care cohort, probable functional hypothalamic amenorrhea was the largest etiological category, followed by PCOS, hypothyroidism and hyperprolactinaemia. Lifestyle, BMI, stress and dietary factors were significantly associated

with probable FHA, while BMI showed a strong association with PCOS. A detailed history, focused examination and basic investigations can identify a substantial proportion of cases. Early lifestyle counselling and correction of modifiable factors should accompany targeted treatment of endocrine disorders, with further evaluation reserved for persistent or atypical cases.

ACKNOWLEDGEMENTS

The authors acknowledge the department of obstetrics and gynecology, Jawaharlal Nehru Hospital and Research Centre, Bhilai, for institutional support, and all study participants for their cooperation.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee of Jawaharlal Nehru Hospital and Research Centre, Bhilai

REFERENCES

- Practice Committee of the American Society for Reproductive Medicine. Current evaluation of amenorrhea: a committee opinion. *Fertil Steril.* 2024;121:679-700.
- Hoffman BL, Schorge JO, Bradshaw KD, Halvorson LM, Schaffer JJ, Corton MM. *Williams Gynecology.* 4th ed. New York: McGraw-Hill; 2020.
- Pinkerton JV. Amenorrhea. *MSD Manual Professional Edition.* Revised 2023. Available from: <https://www.msmanuals.com/professional/gynecology-and-obstetrics/menstrual-abnormalities/amenorrhea>. Accessed on 7 April 2026.
- Gordon CM, Ackerman KE, Berga SL, Kaplan JR, Mastorakos G, Misra M, et al. Functional hypothalamic amenorrhea: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab.* 2017;102:1413-39.
- 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;37:1049-56.
- Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, et al. Recommendations from the 2023 international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Fertil Steril.* 2023;120:633-46.
- Ajmani NS, Sarbhai V, Yadav N, Paul M, Ahmad A, Ajmani AK. Role of thyroid dysfunction in patients with menstrual disorders in tertiary care center of Walled City of Delhi. *J Obstet Gynaecol India.* 2016;66:115-9.
- Biller BMK, Luciano A, Crosignani PG, Molitch M, Olive D, Rehan V, et al. Guidelines for the diagnosis and treatment of hyperprolactinemia. *J Reprod Med.* 1999;44(12):1075-84.
- Majumdar A, Mangal NS. Hyperprolactinemia. *J Hum Reprod Sci.* 2013;6:168-75.
- Mörö S, Kosola S, Holopainen E. Girls referred for amenorrhea: analysis of a patient series from a specialist center. *Front Public Health.* 2024;12:1304277.
- Kafeel H, Rukh R, Zubair A, Ghazala A, Muzaffar H, Raees H, et al. Prevalence and factors associated with functional secondary amenorrhea. *Int J Pharm.* 2014;4(1):16-21.
- Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod.* 2018;33:1602-18.
- Nidhi R, Padmalatha V, Nagarathna R, Amritanshu R. Prevalence of polycystic ovarian syndrome in Indian adolescents. *J Pediatr Adolesc Gynecol.* 2011;24:223-7.
- Rajiwade SR, Sagili H, Soundravally R, Subitha L. Endocrine abnormalities in adolescent girls with menstrual disorders. *J Obstet Gynaecol India.* 2018;68:301-6.
- Lee DY, Oh YK, Yoon BK, Choi D. Prevalence of hyperprolactinemia in adolescents and young women with menstruation-related problems. *Am J Obstet Gynecol.* 2012;206:213.e1-5.
- Raber W, Gessl A, Nowotny P, Vierhapper H. Hyperprolactinemia in hypothyroidism: clinical significance and impact of TSH normalization. *Clin Endocrinol (Oxf).* 2003;58:185-91.
- Chen L, Lu Y, Wang Y, Zhan HF, Zhao YT, Wang YL, et al. The effects of weight loss-related amenorrhea on women's health and the therapeutic approaches: a narrative review. *Transl Pediatr.* 2022;11:1478-88.
- Than WW, Parash MT, Majeed NB, Yin KN, Baharuddin DM, Fahmy EH, et al. A case-control study on factors associated with secondary amenorrhea among the medical students of Universiti Malaysia Sabah. *Cureus.* 2023;15(10).
- Attia GM, Alharbi OA, Aljohani RM. The impact of irregular menstruation on health: a review of the literature. *Cureus.* 2023;15:e49146.
- Dhar S, Mondal KK, Bhattacharjee P. Influence of lifestyle factors with the outcome of menstrual disorders among adolescents and young women in West Bengal, India. *Sci Rep.* 2023;13:12476.
- Karout N, Hawai SM, Altuwairji S. Prevalence and patterns of menstrual disorders among Lebanese nursing students. *East Mediterr Health J.* 2012;18:345-9.
- Bachmann GA, Kemmann E. Prevalence of oligomenorrhea and amenorrhea in a college population. *Am J Obstet Gynecol.* 1982;144:98-102.
- Reindollar RH, Novak M, Tho SP, McDonough PG. Adult-onset amenorrhea: a study of 262 patients. *Am J Obstet Gynecol.* 1986;155:531-43.
- Kumari P, Aggarwal R, Chaudhary S, Shah K. Etiological evaluation of amenorrhea: a cross-

sectional study from a tertiary care center in India. *Int J Reprod Contracept Obstet Gynecol.* 2025;14(1):133-7.

25. Shrivastava P, Vidhyarthi A, Shrivastava RK. Secondary amenorrhea: causes, management and outcome using algorithmic approach. *IOSR J Dent Med Sci.* 2018;17(4):1-5.

Cite this article as: Gupta H, Swathi PS, Kamra S. Analysis of secondary amenorrhea in reproductive age group: a prospective observational study. *Int J Reprod Contracept Obstet Gynecol* 2026;15:4436-42.