Original Article

Comprehensive Assessment of Hormonal Disruption in Primary Amenorrhea

Naheed Shah[1], Samia Saliha[2], Sheeba Jan[3], Zarina Naz[4], Zainab Tahir[5], Hira Arshad[6]

[1] Department of Zoology, University of Sindh, Jamshoro, Pakistan

[2] Maryam Memorial Hospital, Rawalpindi, Pakistan

[3] Department of Obstetrics and Gynecology, Kuwait Teaching Hospital, Peshawar, Pakistan

[4] National Institute of Medical Sciences, Rawalpindi, Pakistan

[5] Sheikh Zayed Hospital, University of Health Sciences, Lahore, Pakistan

[6] Department of Obstetrics and Gynecology, Fouji Foundation Hospital, Rawalpindi, Pakistan

*** Correspondence: Naheed Shah, naheed.shah@usindh.edu.pk**

ABSTRACT

Background: Primary amenorrhea is a heterogeneous condition reflecting disorders of hypothalamic–pituitary–ovarian function or reproductive tract development, and delayed presentation is common in resource-variable settings. Objective: To determine hormonal patterns and etiological distribution of primary amenorrhea among females presenting to tertiary care hospitals in South Punjab, Pakistan. Methods: This observational cross-sectional study enrolled 58 females with primary amenorrhea over two months. Clinical evaluation included demographics, BMI, Tanner breast staging, and pelvic ultrasonography. Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, prolactin, and thyroid-stimulating hormone (TSH) were measured using chemiluminescent immunoassays. Participants were stratified by FSH into hypogonadotropic (<3 mIU/mL), eugonadotropic (3–10 mIU/mL), and hypergonadotropic (>40 mIU/mL) categories. Etiology was determined using integrated clinical, biochemical, and imaging findings. Results: Mean age was 17.4 ± 2.1 years. Eugonadotropic amenorrhea was most common (44.8%), followed by hypogonadotropic (31.0%) and hypergonadotropic amenorrhea (24.1%). Outflow tract anomalies were the leading etiology (36.2%), followed by ovarian disorders (24.1%), hypothalamic–pituitary dysfunction (20.7%), and PCOS (12.1%). Eugonadotropic patients had the highest mean estradiol, while hypergonadotropic cases had markedly reduced estradiol. Conclusion: Structural and ovarian etiologies predominated, and hormonal stratification combined with ultrasonography supported pragmatic etiological triage and management planning.

Keywords: *Primary amenorrhea; Estradiol; Follicle-stimulating hormone; Gonadotropins; Hypogonadism; Outflow tract anomalies; Ovarian disorders; Polycystic ovary syndrome.*

INTRODUCTION

Primary amenorrhea is a sentinel reproductive disorder of adolescence, defined as failure to attain menarche by 15 years in individuals with normal secondary sexual characteristics, or by 13 years in those without pubertal development, and it constitutes a clinically significant indicator of disruption in pubertal progression and reproductive maturation (1). Beyond the absence of menstruation, it reflects potential dysfunction across the hypothalamic–pituitary–ovarian (HPO) axis, failure of end-organ responsiveness, or congenital structural abnormalities of the genital tract, each carrying distinct implications for fertility potential, bone health, psychosocial wellbeing, and long-term endocrine morbidity (2). The diagnostic complexity arises from the fact that menstrual initiation is the final outcome of a precisely regulated hormonal cascade in which pulsatile gonadotropin-releasing hormone (GnRH) secretion stimulates pituitary gonadotropin release, driving folliculogenesis and estradiol production that enables secondary sexual development, endometrial proliferation, and menstrual bleeding (3). Interruption at any stage of this cascade—whether through central suppression, gonadal failure, or an outflow obstruction—can result in an identical clinical

Received: 06 October 2025
Revised: 02 November 2025
Accepted: 26 December 2025
Published: 31 December 2025

Citation: Click to Cite

endpoint of absent menses, necessitating a structured etiological approach rooted in hormonal pattern recognition and anatomical assessment (4).

From a clinical perspective, etiologies of primary amenorrhea are commonly grouped into hypogonadotropic hypogonadism (central GnRH or gonadotropin deficiency), hypergonadotropic hypogonadism (primary ovarian insufficiency or gonadal dysgenesis), and eugonadotropic amenorrhea in which gonadotropins are in the normal range but menstruation is absent because of anatomical outflow tract abnormalities, disorders of sexual development, or endocrine conditions such as polycystic ovary syndrome (PCOS) (1,4). This endocrine stratification is clinically practical because it allows early triage: hypergonadotropic patterns strongly suggest ovarian failure requiring prompt estrogen replacement to mitigate osteopenia and cardiovascular risk, whereas hypogonadotropic patterns prompt evaluation for functional suppression (stress, undernutrition, excessive physical activity), pituitary pathology, chronic systemic disease, or congenital GnRH deficiency syndromes, all of which require fundamentally different management pathways (2,5). In contrast, eugonadotropic primary amenorrhea often raises suspicion for congenital reproductive tract anomalies, including uterovaginal agenesis or obstructive anomalies, in which ovarian function may be preserved and diagnosis depends heavily on pelvic imaging (4,6). Therefore, baseline hormonal profiling combined with ultrasonographic assessment is widely recommended as the cornerstone of initial evaluation in adolescent and young adult females presenting with primary amenorrhea (1,2).

The etiological distribution of primary amenorrhea varies globally and is influenced by referral setting, genetic predisposition, nutritional status, and access to early diagnostic care (4,5). Regional patterns may also reflect sociocultural and population factors such as consanguinity, which can increase the burden of inherited reproductive disorders and congenital anomalies, and delayed care-seeking due to stigma and limited reproductive health awareness (6). However, despite the clinical importance of timely diagnosis, comprehensive Pakistani evidence integrating structured hormonal stratification with ultrasonographic assessment remains limited, particularly from South Punjab where tertiary care hospitals frequently serve as the primary point of evaluation for adolescents presenting late with established amenorrhea and variable pubertal development. Available regional literature often emphasizes either clinical presentations or isolated etiologies but provides insufficient mapping of endocrine patterns aligned with diagnostic categories, limiting the ability to optimize locally relevant diagnostic pathways and counseling (7). This gap is clinically consequential because reliance on external diagnostic algorithms without region-specific validation may lead to unnecessary investigations, delays in etiological identification, or inadequate counseling regarding prognosis, fertility options, and long-term health risks (1,2,7).

In addition, emerging evidence indicates that disorders traditionally associated with secondary amenorrhea, particularly PCOS, may occasionally present as primary amenorrhea in severe early-onset phenotypes, especially in populations with increasing metabolic risk burdens (5,8). This presentation requires careful diagnostic framing because adolescent diagnostic standards for PCOS demand exclusion of physiologic pubertal anovulation and necessitate compatible clinical and/or biochemical hyperandrogenism, making endocrine evaluation and imaging interpretation crucial for avoiding misclassification (8). Consequently, population-specific characterization of hormonal patterns among primary amenorrhea patients is needed not only to clarify the dominant etiologies but also to refine interpretive thresholds for gonadotropins and estradiol levels, contextualize imaging findings, and strengthen clinical decision-making regarding targeted investigations such as karyotyping or pituitary neuroimaging when indicated (1,2).

Accordingly, this study was designed to characterize the hormonal patterns and etiological spectrum of primary amenorrhea among females presenting to tertiary care hospitals in South Punjab, Pakistan, using an integrated assessment of clinical characteristics, secondary sexual development, biochemical hormone profiling, and pelvic ultrasonography. The central research question was whether distinct hormonal strata based on gonadotropin and estradiol profiles correspond to predictable etiological categories in this regional cohort, thereby supporting a pragmatic diagnostic framework for earlier and more accurate etiological identification and counseling in resource-variable clinical settings. (1,2,7)

MATERIALS AND METHODS

This observational cross-sectional study was conducted over a two-month period in the gynecology and endocrinology outpatient departments of tertiary care hospitals in South Punjab, Pakistan. Female patients presenting with primary amenorrhea were assessed for eligibility. Primary amenorrhea was operationally defined as the absence of menarche by 15 years of age in individuals with normal secondary sexual characteristics, or by 13 years of age in those without secondary sexual development, consistent with standard clinical definitions used in adolescent gynecology and endocrinology practice (1,2). Only participants of Pakistani origin who provided informed consent were enrolled. Patients with a history of pelvic radiation, chemotherapy, prior uterine or ovarian surgery, or previously diagnosed chromosomal abnormalities were excluded to minimize confounding from iatrogenic or pre-established etiologies.

Participants were enrolled during the study period using a structured clinical evaluation protocol. Demographic and clinical data were recorded on a standardized proforma, including age, body mass index (BMI), parental consanguinity, and family history of menstrual disorders. Anthropometric measurements were obtained using calibrated instruments, and BMI was calculated as weight in kilograms divided by height in meters squared. Secondary sexual characteristics were assessed through Tanner breast staging by trained clinicians and were categorized as absent (B1) or present (B2–B5) to facilitate clinically meaningful stratification in relation to endocrine status (1,3). Pelvic ultrasonography was performed for all participants by an experienced radiologist to assess uterine presence, uterine morphology, vaginal structure, ovarian size, and ovarian morphology. Ultrasonographic findings were interpreted in conjunction with clinical and biochemical parameters as part of etiological classification.

Venous blood samples were collected in the early morning under fasting conditions to reduce diurnal variability in endocrine measurements. Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, prolactin, and thyroid-stimulating hormone (TSH) were measured using standardized chemiluminescent immunoassay techniques in a certified laboratory with established internal quality controls. Hormonal stratification was performed primarily using FSH concentrations into three diagnostic strata: hypogonadotropic (<3 mIU/mL), eugonadotropic (3–10 mIU/mL), and hypergonadotropic (>40 mIU/mL). Participants were subsequently assigned a final etiological diagnosis based on an integrated interpretation of clinical phenotype, breast development status, biochemical profile, and pelvic ultrasonography. Etiological categories included outflow tract anomalies, ovarian disorders, hypothalamic–pituitary dysfunction, polycystic ovary syndrome (PCOS), and other causes. In the eugonadotropic stratum, PCOS was classified as a distinct category when ultrasonography demonstrated polycystic ovarian morphology together with a compatible gonadotropin–estradiol profile, as described in contemporary endocrine practice; however, classification was restricted to the diagnostic parameters available within the study protocol (8).

Data were entered and analyzed using SPSS. Continuous variables were summarized as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Where comparative analyses across hormonal strata were applicable, one-way analysis of variance (ANOVA) was used for continuous variables, and effect size was quantified using eta-squared (η^2). Proportions were presented with 95% confidence intervals (CIs) using Wilson's method to improve interpretability for clinical decision-making. A two-sided p-value <0.05 was considered statistically significant. Ethical principles consistent with human subject research standards were followed throughout the study, and confidentiality was maintained during data collection and reporting (1,2).

RESULTS

A total of 58 participants meeting the eligibility criteria were enrolled during the two-month study period. The cohort had a mean age of 17.4 ± 2.1 years (range 14–22 years), and the mean BMI was 22.1 ± 4.3 kg/m². Underweight status was observed in 15.5% (n=9), while 24.1% (n=14) were overweight or obese. Parental consanguinity was reported in 34.5% (n=20), and 19.0% (n=11) reported a family history of menstrual disorders. Secondary sexual characteristics were present in 70.7% (n=41), while 29.3% (n=17) had absent breast development (Tanner stage B1), indicating a substantial subgroup with delayed or absent pubertal maturation (Table 1).

Initial hormonal stratification using FSH levels showed that eugonadotropic amenorrhea was the most common hormonal pattern at 44.8% (n=26; 95% CI: 32.7–57.5), followed by hypogonadotropic amenorrhea at 31.0% (n=18; 95% CI: 20.6–43.8) and hypergonadotropic amenorrhea at 24.1% (n=14; 95% CI: 15.0–36.5) (Table 2). No participant fell within the intermediate FSH range (10–40 mIU/mL) under the applied stratification thresholds.

Mean endocrine profiles differed substantially across FSH strata (Table 3). As expected, the hypergonadotropic stratum had markedly elevated mean FSH (68.4 ± 22.1 mIU/mL) and LH (32.5 ± 10.8 mIU/mL), accompanied by suppressed estradiol (15.2 ± 8.1 pg/mL), consistent with ovarian insufficiency physiology. The hypogonadotropic stratum demonstrated low gonadotropins (FSH 1.8 ± 0.5 mIU/mL; LH 1.2 ± 0.6 mIU/mL) and low estradiol (20.8 ± 9.7 pg/mL), aligning with central HPO-axis suppression patterns. The eugonadotropic stratum showed comparatively higher estradiol concentrations (48.5 ± 15.3 pg/mL), consistent with preserved ovarian estrogen output in many cases. Statistical comparison across strata demonstrated highly significant differences for LH ($p<0.001$; $\eta^2=0.842$) and estradiol ($p<0.001$; $\eta^2=0.615$), while prolactin and TSH did not differ significantly between strata ($p=0.386$ and $p=0.678$, respectively), indicating that hyperprolactinemia and thyroid dysfunction were not dominant differentiators in this cohort.

Final etiological classification revealed that outflow tract anomalies were the most frequent diagnosis at 36.2% (n=21; 95% CI: 25.1–49.1), followed by ovarian disorders at 24.1% (n=14; 95% CI: 15.0–36.5), hypothalamic–pituitary dysfunction at 20.7% (n=12; 95% CI: 12.3–32.8), and PCOS at 12.1% (n=7; 95% CI: 6.0–22.9), while other causes accounted for 6.9% (n=4; 95% CI: 2.7–16.4) (Table 4). Ultrasonographic findings were concordant with etiological grouping: outflow tract anomaly cases demonstrated absent uterus and/or vaginal structural abnormalities, ovarian disorder cases showed reduced ovarian size or streak morphology, and PCOS cases exhibited polycystic ovarian morphology.

Table 1. Demographic and Clinical Characteristics of the Study Cohort (N=58)

Characteristic	Value
Age (years)	
Mean ± SD	**17.4 ± 2.1**
Range	**14–22**

Characteristic	Value
BMI (kg/m²)	
Mean ± SD	**22.1 ± 4.3**
Underweight (<18.5), n (%)	**9 (15.5)**
Normal (18.5–24.9), n (%)	**35 (60.3)**
Overweight/Obese (≥25), n (%)	**14 (24.1)**
Family history and genetics	
Parental consanguinity, n (%)	**20 (34.5)**
Family history of menstrual disorders, n (%)	**11 (19.0)**
Secondary sexual characteristics	
Tanner B1 (Absent), n (%)	**17 (29.3)**
Tanner B2–B5 (Present), n (%)	**41 (70.7)**

Table 2. Initial Hormonal Stratification Based on FSH Levels (N=58)

Diagnostic stratum	FSH range (mIU/mL)	n (%)	95% CI for proportion
Hypogonadotropic	**<3**	**18 (31.0)**	**20.6–43.8**
Eugonadotropic	**3–10**	**26 (44.8)**	**32.7–57.5**
Hypergonadotropic	**>40**	**14 (24.1)**	**15.0–36.5**

95% CI calculated using Wilson's method.

Table 3. Mean Hormonal Profile by FSH Stratum With Between-Group Comparisons (ANOVA)

Hormone (unit)	Hypogonadotropic (n=18)	Eugonadotropic (n=26)	Hypergonadotropic (n=14)	p-value	Effect size (η^2)
FSH (mIU/mL)	**1.8 ± 0.5**	**5.9 ± 1.7**	**68.4 ± 22.1**	**—***	**—***
LH (mIU/mL)	**1.2 ± 0.6**	**6.1 ± 2.3**	**32.5 ± 10.8**	**<0.001**	**0.842**
Estradiol (pg/mL)	**20.8 ± 9.7**	**48.5 ± 15.3**	**15.2 ± 8.1**	**<0.001**	**0.615**
Prolactin (ng/mL)	**14.1 ± 6.2**	**16.5 ± 7.8**	**13.8 ± 5.9**	**0.386**	**0.034**
TSH (µIU/mL)	**2.1 ± 0.9**	**2.3 ± 1.0**	**2.4 ± 1.1**	**0.678**	**0.014**

FSH is the stratifying variable; inferential testing across strata is not applicable as group formation was determined by FSH thresholds.

Table 4. Final Etiological Distribution of Primary Amenorrhea (N=58)

Etiology	n (%)	95% CI for proportion
Outflow tract anomalies	**21 (36.2)**	**25.1–49.1**
Ovarian disorders	**14 (24.1)**	**15.0–36.5**
Hypothalamic–pituitary dysfunction	**12 (20.7)**	**12.3–32.8**
PCOS	**7 (12.1)**	**6.0–22.9**
Other causes	**4 (6.9)**	**2.7–16.4**

95% CI calculated using Wilson's method.

Across FSH-stratified phenotypes of primary amenorrhea, a marked nonlinear hormonal gradient was observed, demonstrating distinct endocrine signatures supporting etiological triage. Mean LH increased progressively from 1.2 ± 0.6 mIU/mL in the hypogonadotropic group to 6.1 ± 2.3 mIU/mL in the eugonadotropic group and peaked at 32.5 ± 10.8 mIU/mL in the hypergonadotropic group, indicating strong axis activation in ovarian failure states.

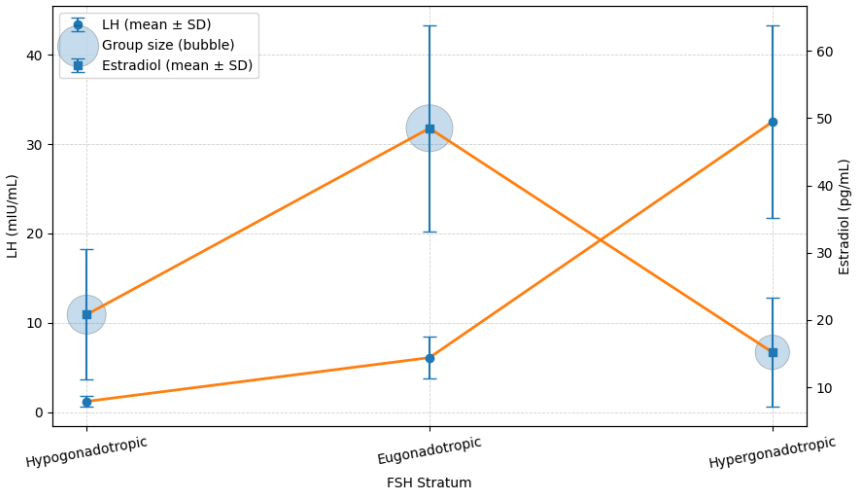

Figure 1 Gonadotropin–Estradiol Gradient Across FSH-Stratified Primary Amenorrhea Phenotypes

In contrast, estradiol demonstrated an inverted pattern, reaching its highest level in the eugonadotropic phenotype (48.5 ± 15.3 pg/mL) compared with 20.8 ± 9.7 pg/mL in hypogonadotropic and 15.2 ± 8.1 pg/mL in hypergonadotropic amenorrhea, reflecting

preserved ovarian steroidogenesis in the eugonadotropic group but marked estrogen deficiency in hypergonadotropic cases. Sample-size overlay showed the largest concentration in the eugonadotropic stratum (n=26), reinforcing that structural or functional eugonadotropic etiologies constitute the dominant clinical presentation in this cohort.

DISCUSSION

This study delineates the hormonal and etiological spectrum of primary amenorrhea in a tertiary-care cohort from South Punjab, Pakistan, highlighting the diagnostic value of endocrine stratification integrated with pelvic ultrasonography. The predominance of eugonadotropic amenorrhea, followed by hypogonadotropic and hypergonadotropic patterns, supports the clinical principle that primary amenorrhea is not a single entity but rather a shared clinical endpoint emerging from distinct pathophysiologic pathways across the HPO axis and reproductive tract development (9). In this cohort, the eugonadotropic stratum comprised nearly half of the cases and demonstrated the highest mean estradiol concentration, implying preserved ovarian steroidogenesis in a large subgroup. This pattern is classically consistent with structural etiologies—particularly uterovaginal anomalies and obstructive conditions—where menstruation is absent despite ovarian function, making imaging an indispensable component of first-line workup (10). The finding that outflow tract anomalies represented the largest etiologic category aligns with reports from referral-based adolescent gynecology settings, where congenital tract anomalies are frequently detected once menstruation fails to occur despite secondary sexual maturation (11). Importantly, this reinforces the need to prioritize pelvic ultrasonography early, especially in patients with normal breast development and eugonadotropic hormone profiles, to reduce diagnostic delays and unnecessary endocrine testing.

The hypergonadotropic group exhibited a marked elevation of gonadotropins accompanied by suppressed estradiol, a hormonal signature strongly suggestive of primary ovarian insufficiency or gonadal dysgenesis. This endocrine phenotype carries implications beyond reproductive capacity, including long-term skeletal and cardiometabolic risks, and thus requires early diagnosis and structured management through hormone replacement, bone health monitoring, and fertility counseling (9,12). Although detailed genetic confirmation was not performed in this cohort, contemporary evidence emphasizes that chromosomal and genetic etiologies contribute substantially to hypergonadotropic primary amenorrhea, and karyotyping remains critical where feasible to refine diagnosis and guide patient counseling, including assessment of tumor risk in specific disorders of sex development (12–14). Similarly, the hypogonadotropic stratum demonstrated low gonadotropins and low estradiol, consistent with hypothalamic–pituitary dysfunction. This category requires a fundamentally different diagnostic pathway, including evaluation for functional hypothalamic suppression, systemic illness, and pituitary lesions, with neuroimaging considered when clinical features or endocrine patterns suggest organic pathology (9). These findings collectively underscore the clinical utility of early gonadotropin and estradiol profiling to triage patients into evidence-based investigative pathways rather than applying uniform, resource-intensive panels.

A clinically noteworthy finding was the identification of a subset categorized as PCOS among primary amenorrhea presentations. While PCOS is traditionally associated with oligomenorrhea or secondary amenorrhea, severe early-onset phenotypes may present with absent menarche, particularly in settings where metabolic risk and adolescent endocrine dysfunction are increasingly recognized (15). However, PCOS diagnosis in adolescents demands stringent criteria and careful exclusion of physiologic pubertal anovulation; therefore, in resource-limited settings, such classifications should be interpreted cautiously

unless supported by clinical and/or biochemical hyperandrogenism alongside persistent ovulatory dysfunction and compatible imaging findings (15,16). Nonetheless, the presence of a eugonadotropic subgroup with relatively higher estradiol levels and polycystic ovarian morphology suggests that PCOS-like endocrine patterns may meaningfully contribute to primary amenorrhea presentations in the region and merits further investigation through standardized adolescent diagnostic frameworks and expanded hormonal assessment (15,16).

The study also provides contextual relevance through observed consanguinity rates, which may influence the regional burden of congenital reproductive disorders and hereditary endocrine conditions. Although causal inference is not possible from this design, these findings support the rationale for incorporating family history and consanguinity assessment into clinical evaluation and for advancing population-specific genetic research in amenorrhea and infertility pathways (13,14). The strengths of this work include the protocol-based integration of clinical examination, Tanner staging, standardized hormone assays, and pelvic ultrasonography, enabling a pragmatic etiological classification aligned with real-world diagnostic workflows. However, key limitations must be acknowledged. The cross-sectional design limits etiological refinement over time, the modest sample size constrains precision for less common causes, and the tertiary-care setting introduces referral bias, potentially over-representing structural and severe endocrine etiologies relative to community populations (11).

Additionally, the absence of universal karyotyping, pituitary imaging, and broader endocrine panels restricts definitive classification in subsets where genetic or central etiologies may overlap (12–14). Future multicenter Pakistani studies should incorporate standardized diagnostic protocols including genetic testing where indicated, longitudinal follow-up to evaluate outcomes, and refined diagnostic criteria for adolescent PCOS to prevent misclassification while capturing true severe phenotypes (15,16).

CONCLUSION

In this tertiary-care cohort from South Punjab, Pakistan, primary amenorrhea most frequently resulted from outflow tract anomalies and ovarian disorders, with hormonal stratification revealing distinct endocrine profiles that meaningfully supported etiological triage and diagnostic planning. The predominance of eugonadotropic patterns with higher estradiol levels emphasizes the importance of early pelvic imaging for timely identification of structural causes, while hypergonadotropic and hypogonadotropic profiles highlight the need for targeted evaluation for ovarian failure and central HPO-axis dysfunction, respectively.

These findings support a combined clinical–biochemical–imaging framework as a practical diagnostic pathway in resource-variable settings and justify larger multicenter studies incorporating genetic and advanced endocrine evaluation to refine regional protocols, improve counseling, and optimize long-term reproductive and metabolic outcomes.

DECLARATIONS

Ethical Approval
Ethical approval was taken from respective institutions of data collection placements.
Informed Consent
Informed Consent was taken from participants
Conflict of Interest
The authors declare no conflict of interest.
Funding
This research received no external funding.

DECLARATIONS

Authors' Contributions

Concept: NS; Design: NS, SS; Data Collection: SJ, ZN, ZT, HA; Analysis: NS, SS; Drafting: NS, SS, SJ, ZN, ZT, HA

Data Availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Acknowledgments

Not applicable.

Study Registration

Not applicable.

REFERENCES

1. Gaspari L, Paris F, Kalfa N, Sultan C. Primary amenorrhea in adolescents: approach to diagnosis and management. Endocrines. 2023;4(3):536–547.
2. Gaspari L, Paris F, Kalfa N, Sultan C. Primary amenorrhea in adolescents: approach to diagnosis and management. Endocrines. 2023;4:536–547.
3. Anthon C, Steinmann M, Vidal A, Dhakal C. Menstrual disorders in adolescence: diagnostic and therapeutic challenges. J Clin Med. 2024;13(24):7668.
4. Deo S, Singh S, Kumari P, Agarwal M, Ali W, Nigam N. Evaluation of etiopathology and management of primary and secondary amenorrhea in adolescent and young women in North Indian population. 2024.
5. Adão ML. Evaluation and management of primary amenorrhea. 2024.
6. Lewis V. Reproductive endocrinology and infertility. Boca Raton: CRC Press; 2024.
7. Christopoulos P, Vatopoulou A, Michala L, Nižňanská Z, Stankovic Z, Roos E, et al. Abstracts of the 16th European Congress of Paediatric and Adolescent Gynaecology. J Clin Med. 2024;13(24):7574.
8. Memi E, Pavli P, Papagianni M, Vrachnis N, Mastorakos G. Diagnostic and therapeutic use of oral micronized progesterone in endocrinology. Rev Endocr Metab Disord. 2024;25(4):751–772.
9. Ioannou D, Tempest HG. The genetic basis of male and female infertility. Semin Biol Reprod Med. 2025;71(1):143–169.
10. Zuhairi AK, Almomin AM, Alhubaish E, Mansour AA, Zuhairi AJ. The spectrum of hypogonadism in women from Basrah. Cureus. 2024;16(8).
11. Pan J, Liu P, Yu X, Zhang Z, Liu J. The adverse role of endocrine disrupting chemicals in the reproductive system. Front Endocrinol. 2024;14:1324993.
12. Ishii T, Kashimada K, Kawai M, Itonaga T, Iwasa T, Utsunomiya A, et al. Clinical practice guidelines for the management of differences of sex development in Japan. 2025.
13. Dashti Z, Falahi J, Parsanejad M. Reproductive genetics. Eur J Hum Genet. 2024;32:349–795.
14. Kalapahar S, Sharma S, Chattopadhyay R, Karan M. Overview of genetics in infertility. Bull Inst Reprod Med. 2024;39.
15. Van der Kelen A. The impact of genetics on reproductive medicine. 2024.

16. Mordovina II, Chebanu AK, Donnikov MY, Sinyukova TA, Kovalenko LV, Belotserkovtseva LD, et al. Genetic factors of reproductive disorders in female. 2024;8(03):186–195.

17. Khatun H, Halim T, Ferdous B, Rahman R, Hasan MM, Khan A. Prevalence of etiologic causes of primary amenorrhea among women in a tertiary care center. Sci Int J Obstet Gynecol. 2024;7(11):573–578.

18. Tiffany A. Exploring the heterogeneous genetic origin of female subfertility [thesis]. Ghent University; 2024.

19. Yalçın SFT. e-Posters EP01 cancer genetics. 2024.

20. Delcour C. Exploration des mécanismes étiopathogéniques des pathologies de la puberté [thesis]. Université Paris Cité; 2024.