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Original Research Article

Exploring the Etiology and Management of Primary Amenorrhea: A Comprehensive Study at Tertiary Care Hospital in Visakhapatnam

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Abstract:

Background: Primary amenorrhea, characterized by the absence of menarche by a certain age, presents a complex array of etiologies ranging from genetic abnormalities to hormonal imbalances. Understanding these underlying causes is critical for effective management. The study aimed to explore the etiology, clinical presentation, diagnostic outcomes, and management strategies for primary amenorrhea.

Methods: An observational study was conducted at a tertiary care hospital in Visakhapatnam from June 2021 to November 2022, involving 25 female patients with primary amenorrhea. Data collection included detailed history-taking, clinical examinations, hormonal assessments, ultrasound imaging, and karyotyping. Statistical analysis was performed using Excel, focusing on demographic characteristics and diagnostic outcomes.

Results: The study revealed a diverse range of presentations and underlying causes of primary amenorrhea. Swyer Syndrome and androgen insensitivity syndrome were among the identified etiologies, emphasizing the complexity of the condition. Individualized diagnostic and therapeutic approaches were crucial for effective management. Surgical interventions, hormonal therapy, and genetic counselling were implemented based on the specific diagnosis.

Conclusion: A multidisciplinary approach integrating clinical evaluation, imaging studies, and genetic testing is essential for diagnosing and managing primary amenorrhea effectively. Early detection and intervention are paramount to prevent complications and improve patient outcomes. Continued research and collaboration among healthcare professionals are recommended to enhance understanding and refine treatment approaches.

Recommendations: It is recommended to prioritize early detection and intervention for primary amenorrhea, employing a comprehensive diagnostic protocol that includes clinical evaluation, hormonal assays, imaging studies, and genetic testing. Furthermore, collaboration among healthcare professionals from diverse specialties is crucial for providing individualized care and improving patient outcomes.

Keywords: Primary Amenorrhea, Diagnosis, Management, Multidisciplinary Approach.

Introduction

Primary amenorrhea is a medical condition characterized by the absence of menarche by the age of 15 in females who have otherwise developed secondary sexual characteristics or by the age of 13 in the absence of secondary sexual characteristics [1]. This condition is not merely a symptom but a complex manifestation of a variety of potential etiologies, ranging from congenital anomalies to systemic diseases. Understanding the underlying causes is crucial for effective management and treatment.

The etiology of primary amenorrhea is multifaceted, involving chromosomal, anatomical, hormonal, and environmental factors. Chromosomal abnormalities, such as Turner syndrome (45,X) and Androgen Insensitivity Syndrome (AIS), account for a significant proportion of cases, highlighting the role of genetic factors in the development of this condition [2]. Anatomical anomalies, including Müllerian agenesis or imperforate hymen, also contribute to the incidence of primary amenorrhea, underscoring the importance of thorough physical examinations and imaging studies in the diagnostic process [3].

Hormonal imbalances, particularly those involving the hypothalamic-pituitary-ovarian (HPO) axis, can lead to the failure of menstrual cycle initiation. Conditions such as polycystic ovary syndrome (PCOS) and hypogonadotropic hypogonadism are notable examples, which may require hormonal assays for accurate diagnosis [4]. Furthermore, environmental factors and lifestyle choices,

including excessive physical exercise and eating disorders, can also precipitate this condition, suggesting a multifactorial etiology that encompasses both intrinsic and extrinsic factors [5].

Management strategies for primary amenorrhea are tailored to the underlying cause. Chromosomal or genetic abnormalities may benefit from genetic counselling and hormone replacement therapy (HRT) to induce secondary sexual characteristics and menstruation [2]. For anatomical causes, surgical interventions can be effective in creating a patent outflow tract, thereby allowing for normal menstruation [3]. Hormonal imbalances often require pharmacological treatment to restore normal HPO axis function and induce ovulation. Additionally, addressing lifestyle and environmental factors through nutritional counseling and psychological support is crucial for a holistic approach to management [5].

The aim of this study was to explore the etiology, clinical presentation, and diagnostic outcomes of primary amenorrhea. By analyzing demographic profiles, identifying underlying causes through a comprehensive diagnostic approach, and evaluating management strategies, the study sought to enhance understanding and improve patient care for this complex condition.

Methodology

Study Design

This research was conducted as an observational study

Study Setting

The study was carried out at tertiary care hospital in Visakhapatnam, spanned from June 2021 to November 2022, offering a comprehensive view over an 18-month period.

Participants

The study included a total of 25 female patients who presented with primary amenorrhea.

Inclusion criteria

- Females aged >13 years with primary amenorrhea and the absence of secondary sexual characteristics.

- Females aged >15 years with primary amenorrhea, normal growth and development, and the presence of secondary sexual characteristics.

Exclusion criteria

Patients with secondary amenorrhea, those younger than 13 years, or those unwilling to give consent were excluded from the study.

Bias

There was a chance that bias would arise when the study first started, but it was avoided by giving all participants the identical information and hiding the group allocation from the nurses who collected the data.

Variables

Variables included demographic details, clinical symptoms, laboratory parameters, and outcomes.

Data Collection

Data collection involved a detailed history taking, focusing on symptoms that could indicate an obstruction of the outflow tract, the presence of delayed menarche in family history, and the age at thelarche and adrenarche. A comprehensive clinical examination was conducted for each patient, including anthropometric measurements and the assessment of external and internal genitalia. The examination of secondary sexual characteristics was based on the Tanner staging of breast and pubic hair.

Diagnostic Assessments

All patients underwent ultrasound examinations to assess the presence and condition of the uterus, tubes, and ovaries. Further investigations included karyotyping and hormonal analysis to support the clinical findings and ultrasound data. These assessments aimed to develop a diagnostic protocol that facilitates easier diagnosis and prevents misdiagnosis.

Statistical Analysis

The data obtained from the study was arranged in a tabulated manner in an Excel sheet, and the data was then subjected to statistical analysis such as frequency, percentages, etc.

Ethical considerations

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

Result

Table 1: Demographics characteristics of study population

Parameters	Values
Age (years)	
- 14-15	6 (24%)
- 16-20	12 (48%)
- 21-25	4 (16%)
- 26-30	1 (4%)
- 31-35	1 (4%)
Present complaints	
- Amenorrhea	24 (96%)
Associated symptoms	
- Cyclical abdominal pain	6 (24%)
- Mass per abdomen	1 (4%)
- Dyspareunia	1 (4%)

The study on primary amenorrhea included a comprehensive analysis of 25 female patients. These patients underwent a thorough clinical evaluation, hormonal assessments, ultrasound imaging, and karyotyping to elucidate the underlying causes of their condition.

The age of the participants ranged from 14 to 31 years, with a diverse presentation of symptoms and clinical findings. A significant proportion of the patients exhibited symptoms and signs that warranted further investigation for disorders such as Swyer Syndrome, androgen insensitivity syndrome, and other genetic or anatomical abnormalities.

Table 2: Etiology of Primary Amenorrhea

Etiology	Values
Hypergonadotropic hypogonadism	52%
Eugonadotropic eugonadism	48%
Hypogonadotropic hypogonadism	0%
Hyper gonadotropic hypogonadism	52%
Imperforate hymen	20%
Transverse vaginal septum	4%
MRKH syndrome	20%
Incomplete AIS	4%

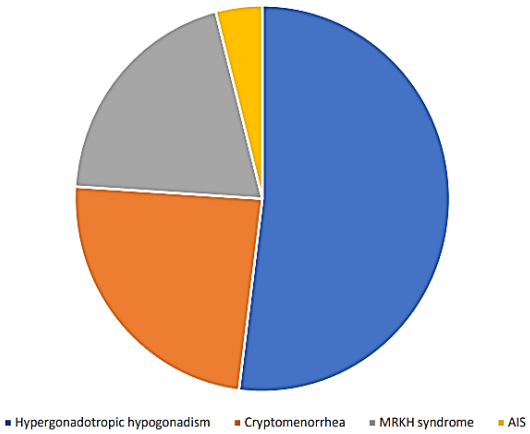

Figure 1: Etiology of Primary Amenorrhea

Swyer Syndrome was diagnosed in 12% of the cases, with 3 out of 25 patients displaying this condition. Two of these patients, both 14 years old, presented with primary amenorrhea and were found to have a 46XY karyotype. They underwent laparoscopic gonadectomy after histopathology confirmed the presence of testicular tissue. Hormonal therapy with estrogen and progesterone was initiated following surgery.

A notable case involved a 31-year-old tribal patient with a history of primary amenorrhea and a physically undeveloped uterus, who was also phenotypically female with a masculine body build. This patient's diagnostic workup, including

karyotyping and CECT scans, led to the diagnosis of Swyer Syndrome. Surgical intervention revealed the absence of a uterus and the presence of a gonadoblastoma on the right side, further complicating the clinical picture.

Androgen insensitivity syndrome was identified in 4% of the study participants, reflecting the diverse etiological spectrum of primary amenorrhea. The study's findings emphasized the importance of a multidisciplinary approach to diagnosing primary amenorrhea, incorporating clinical evaluation, imaging studies, and genetic testing. The varied presentations and underlying causes observed in the patients underscore the necessity for individualized diagnostic and therapeutic strategies.

Discussion

The study on primary amenorrhea among 25 female patients provides significant insights into the complexity and diversity of this condition. The comprehensive diagnostic approach, encompassing clinical evaluation, hormonal assessments, ultrasound imaging, and karyotyping, revealed a broad spectrum of underlying causes, ranging from genetic abnormalities such as Swyer Syndrome and androgen insensitivity syndrome to anatomical anomalies. Gonadal dysgenesis, particularly Swyer Syndrome, emerged as the most common cause for primary amenorrhea in the present study, underscoring the critical role of genetic factors in this condition. Notably, the diagnosis of Swyer Syndrome in 12% of the cases underscores the critical role of genetic factors in primary amenorrhea, with surgical and hormonal interventions being pivotal in the management of such cases.

A particularly complex case of a 31-year-old with Swyer Syndrome highlighted the challenges in diagnosing and treating patients with atypical presentations. The identification of androgen insensitivity syndrome in a smaller fraction of the study group further illustrates the etiological diversity of primary amenorrhea.

This study emphasizes the necessity of a multidisciplinary diagnostic and therapeutic approach to accommodate the wide variability in clinical presentations and underlying pathologies, advocating for personalized treatment plans to address the unique needs of each patient effectively.

Research on primary amenorrhea has revealed diverse etiological factors and emphasized the importance of comprehensive diagnostic approaches. A study from a tertiary care hospital in Western India identified Mullerian agenesis and gonadal dysgenesis as the most common causes of primary amenorrhea, highlighting the varied etiology in the region [6]. Another study associated the FSHR rs6166 G2039A polymorphism with primary amenorrhea, suggesting genetic predispositions as causative risk factors [7]. Cytogenetic evaluations across different regions, including a study of 100 cases at a tertiary center and another in Eastern India, underscored the necessity of cytogenetic analysis for accurate diagnosis and management [8, 9]. In Kerala, a retrospective study found a significant proportion of primary amenorrhea cases were due to cytogenetic abnormalities, advocating for karyotyping as a crucial part of patient evaluation [10]. Lastly, research in Kashmir indicated the essential role of chromosomal analysis after excluding non-genetic causes for precise diagnosis and treatment [11]. Together, these studies reflect the complexity of diagnosing primary amenorrhea and the critical role of genetic and cytogenetic analyses in its management.

Conclusion

In conclusion, the study on primary amenorrhea reveals a diverse etiological spectrum and clinical presentations among female patients, emphasizing the necessity for a multidisciplinary approach in diagnosis and management. Through meticulous evaluation incorporating clinical examinations, hormonal assessments, imaging studies, and genetic testing, various underlying causes such as Swyer Syndrome and androgen insensitivity syndrome were identified. Individualized diagnostic and therapeutic strategies are crucial for addressing the complexity of cases encountered, highlighting the importance of early detection and intervention to prevent potential complications and improve patient outcomes. Continued research and collaboration among healthcare professionals are essential for enhancing our understanding of primary amenorrhea and refining diagnostic and treatment approaches, ultimately prioritizing a comprehensive and patient-centered approach to better meet the needs of affected individuals and improve their overall quality of life.

Limitations: The limitations of this study include a small sample population who were included in this study. The findings of this study cannot be generalized for a larger sample population. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

Recommendation: It is recommended to prioritize early detection and intervention for primary amenorrhea, employing a comprehensive diagnostic protocol that includes clinical evaluation, hormonal assays, imaging studies, and genetic testing. Furthermore, collaboration among healthcare professionals from diverse specialties is crucial for providing individualized care and improving patient outcomes.

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References

1. Committee on Adolescent Health Care. Primary ovarian insufficiency in adolescents and young women. Obstet Gynecol. 2018;132 (1):e35-e41.
2. Azziz R, Carmina E, Chen Z, et al. Polycystic ovary syndrome. Nat Rev Dis Primers. 2016; 2:16057.
3. Gravholt CH, Andersen NH, Conway GS, et al. Clinical practice guidelines for the care of girls and women with Turner syndrome: proceedings from the 2016 Cincinnati International Turner Syndrome Meeting. Eur J Endocrinol. 2019;181(3):G1-G70.
4. Patnaik SS, Brazile B, Dandolu V, Ryan PL, Liao J, Bhattarai S. Anatomical and morphological evaluation of Müllerian duct anomalies: diagnostic value of MRI. J Obstet Gynaecol Res. 2014;40(1):198-206.
5. Warren MP, Chua AT. Clinical manifestations and evaluation of spontaneous primary ovarian insufficiency (premature ovarian failure). UpToDate. Accessed February 7, 2024. https://www.uptodate.com/contents/clinical-manifestations-and-evaluation-of-spontaneous-primary-ovarian-insufficiency-premature-ovarian-failure
6. Malin KJ, Vittner D, Darilek U, McGlothen-Bell K, Crawford A, Koerner R, Pados BF, Cartagena D, McGrath JM, Vance AJ. Application of the Adverse Childhood Experiences Framework to the NICU. Advances in Neonatal Care. 2024 Feb 1;24(1):4-13.
7. Sanghavi P, Chandel D. The Effect of FSHR (G2039A) Polymorphism on Müllerian Duct Development and Hormonal Profile of Women with Primary Amenorrhea. J Reprod Infertil. 2023;24(4):240-247.
8. Pritti, K., Mishra, V., Patel, H. et al. Cytogenetic evaluation of primary amenorrhea: a study of 100 cases at tertiary centre. Egypt J Med Hum Genet 23, 151 (2022).
9. Ghosh S, Roy S, Pal P, Dutta A, Halder A. Cytogenetic analysis of patients with primary amenorrhea in Eastern India. J Obstet Gynaecol. 2018;38(2):270-275.
10. Thankam U, Hariharan SV, Sarojam S, Syamala R, Alex ST, Ratnamma NV, Jacob S. Proportion and Pattern of Chromosomal Abnormalities in Primary Amenorrhoea in Kerala, India- A Retrospective Study. J Clin of Diagn Res. 2022; 16(11):QC09-QC12.
11. Malla TM, Dar FA, Pandith AA, Zargar MH. Frequency and pattern of cytogenetic alterations in primary amenorrhea cases of Kashmir, North India. Egyptian Journal of Medical Human Genetics. 2016;17(1):25-31.