

STUDY OF THE CLINICAL PROFILE AND AETIOLOGY OF PATIENTS WITH PRIMARY AMENORRHEA PRESENTING TO ENDOCRINE OPD OF A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

Amenorrhea refers to the absence of menstrual periods and may result from a number of different conditions. The normal menstrual cycle involves complex interactions between the hypothalamic pituitary axis, the ovaries and the outflow tract, thus disruption at any level can result in abnormal menstruation and amenorrhea. Amenorrhea is broadly classified into primary or secondary. Amenorrhea is classified as primary if menstrual bleeding has never occurred in the absence of hormonal treatment. The clinical significance of lack of regular menstrual cycles extends beyond reproductive concerns and include implications on bone and cardiovascular health.

The aim of this study was to evaluate the clinical profile and etiology, mean age of presentation of common etiologies, common age group of presentation, variation of gonadotropin levels, of patients of primary amenorrhea presenting to Endocrine OPD of a tertiary care hospital.

MATERIALS AND METHODS

We assessed the records of patients who were evaluated for primary amenorrhea by age 16 years in the presence of normal growth and secondary sexual characteristics and patients who were evaluated for absence of secondary sexual characteristics by age 13 with or without short stature, between May 2014 to June 2017 in our Endocrine department. The patients were subjected to a detail history, thorough clinical examination, relevant biochemical, hormonal and radiological investigations as indicated.

Design- Cross-sectional study.

RESULTS

In our study, a total number of 29 patients presented for evaluation during the study period. The mean age of presentation of patients with primary amenorrhea was 20.21±4.08 years. 65% (N=19) of patients presented between 11-20 years and 35% (N=10) presented between 21-30 years. The most common causes of primary amenorrhea were Turner syndrome (45%; N=12) and Mayer-Rokitansky-Kuster-Hauser syndrome (MRKH) (10%, N=3). Among patients with Turner syndrome most common cause for seeking medical evaluation was both primary amenorrhea and short stature rather than short stature alone.

CONCLUSION

In concordance with other studies, Turner syndrome and Mullerian agenesis disorders are the commonest causes of primary amenorrhea in our study. Prolonged untreated hypothyroidism though identified as an important cause of secondary amenorrhea can also present as primary amenorrhea in few cases. Treatment should begin immediately after diagnosis in a patient tailored fashion not only to facilitate normal secondary sexual features and fertility concerns but also to preserve bone and cardiovascular health.

KEYWORDS

Amenorrhea, Turner Syndrome, Mullerian Anomalies.

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BACKGROUND

Amenorrhea refers to the absence of menstrual periods. It is classified into primary and secondary depending upon the onset of time of absent menstrual bleeding. Amenorrhea may result from a number of different conditions hence a thorough knowledge of the physiology of menstruation is essential to understand the various causes of amenorrhea. The normal menstrual cycle involves complex interactions between the hypothalamic-pituitary axis, the ovaries and the

outflow tract. In this complex and highly regulated sequence of events, any disruption or functional abnormality of the hypothalamic-pituitary-ovarian axis can result in abnormal menstruation. Other endocrinological diseases and structural abnormalities of the outflow tract can cause amenorrhea.^{1,2}

Primary amenorrhea refers to cases where menstrual bleeding has never occurred in the absence of hormonal treatment. This is a rare disorder occurring in less than one percent of female population.³ The absence of menses by age 16 has been traditionally used to define primary amenorrhea. However other factors, such as growth, secondary sexual characteristics and secular trend to an earlier age of menarche may also influence the age, at which primary amenorrhea should be investigated. Thus, an evaluation for amenorrhea should be initiated by age 15 or 16 in the presence of normal growth and secondary sexual characteristics, age 13 in the absence of secondary sexual characteristics or if height is less than third percentile or within 2 years of breast development if menarche has not occurred.

The clinical significance of lack of regular menstrual cycles extends beyond reproductive concerns. Episodes of amenorrhea as short as 90 days may have implications for bone and cardiovascular health. Hence prolonged amenorrhea depending upon its underlying etiology, can be a harbinger of substantial cardiovascular risk.⁴

MATERIALS AND METHODS

All consecutive patients with primary amenorrhea by age 16 years in the presence of normal growth and secondary sexual characteristics and patients with absence of secondary sexual characteristics by age 13 with and without short stature, presenting to Endocrinology OPD of S.C.B Medical College, Cuttack from May 2014 to June 2017, were enrolled in the study. A detailed clinical evaluation including history taking was carried out for all patients. They were further subjected to relevant biochemical, hormonal, radiological investigations and karyotyping as indicated. Written and informed consent was taken for each subject or their parents. Institutional ethical committee clearance was taken.

The data was analysed using standard statistical methods. The graphs and tables were generated using Microsoft excel 2007 software.

RESULTS

A total of 29 patients were evaluated in the study period. The mean age of presentation of patients with primary amenorrhea was 20.21 ± 4.08 years. Most of the patients presented between 10-20 years of age (65%, N= 19), followed by age group 21- 30 years (35%, N=10) (Figure 1). The most common etiology of primary amenorrhea was Turner syndrome (41%, N=12) followed by MRKH (10%, N=3). Two patients evaluated for primary amenorrhea had AIS. The other etiologies in descending order of occurrence were isolated hypogonadotropic-hypogonadism (7%, N=2), primary hypothyroidism (7%, N=2), pituitary hypoplasia (4%, N=1), other Mullerian abnormality (4%, N=1),

complete gonadal dysgenesis (4%, N=1), hyperprolactinemia (4%, N=1), constitutional delay in growth and puberty (4%, N=1), 46XX ovotesticular DSD (45%, N=1), celiac disease (4%, N=1) and congenital adrenal hyperplasia (4%, N=1) (Figure 2). The mean age of presentation of major etiologies of primary amenorrhea were Turner syndrome (20 years), MRKH (19 years), isolated hypogonadotropic-hypogonadism (25 years), primary hypothyroidism (24.5 years), complete gonadal dysgenesis (22 years), CDGP (17 years) and other mullerian abnormality (18 years) respectively (Figure 3). Gonadotropins estimation revealed 6 patients who had hypogonadotropic-hypogonadism and 20 patients who had hypergonadotropic-hypogonadism. Three patients had gonadotropin values which were in normal ranges (Figure 4).

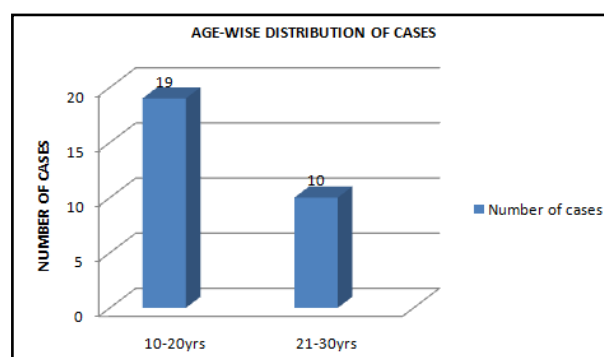


Figure 1. Graph Showing Age-wise Distribution of Cases

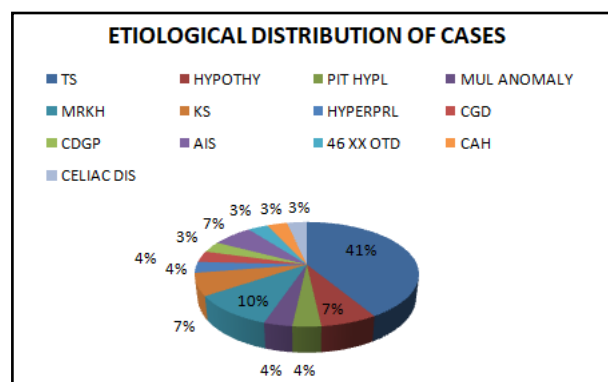


Figure 2. Pie Chart Showing the Etiological Distribution of Cases

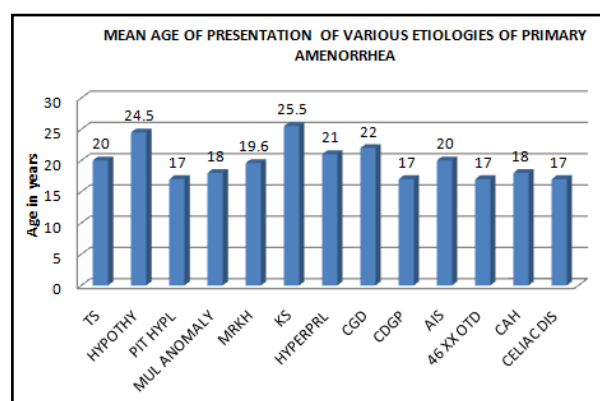


Figure 3. Graph Showing the mean Age of Presentation of Various Etiologies of Primary Amenorrhea

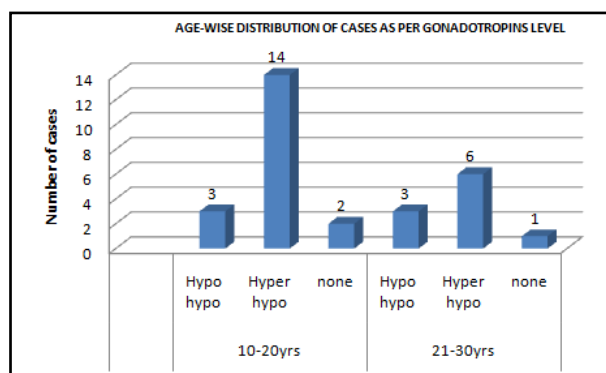


Figure 4. Graph Showing the Age-wise Distribution of Cases with Relation to Gonadotropins Level

DISCUSSION

Research in reproduction continues to provide critical insights into our knowledge of the mechanism responsible for amenorrhea in women. Among various cause of primary amenorrhea, the majority of causes likely remains unchanged with the four most common causes of primary amenorrhea being ovarian failure (48.5%), congenital absence of uterus and vagina (16.2%), GnRH deficiency (8.3%) and constitutional delay of puberty (6.0%).⁵ In prior studies one done in Thailand in 2009, the three most common causes of primary amenorrhea were Mullerian agenesis (39.7%), gonadal dysgenesis (35.3%), and hypogonadotropic-hypogonadism.⁶ In a study reported by Bhuyan et al, the mean age of presentation for primary amenorrhea was 17.23 ± 4.2 years. In the mentioned study which included fourteen patients the most common causes of primary amenorrhea were Turner syndrome (35.71%), Mullerian agenesis (14.28%), 46XX (pure) gonadal dysgenesis (14.28%), 46 XY gonadal dysgenesis (14.28%), hypothalamic amenorrhea (14.28%) and MPRD (7.14%). In our study, the mean age of presentation was 20.21 ± 4.08 years. The common causes were Turner syndrome followed by Mullerian agenesis in concordance with other studies. Among 12 patients with Turner syndrome, 9 patients presented for evaluation of both primary amenorrhea and short stature rather than short stature alone, whereas the other 3 presented for poor development of secondary sexual features and primary amenorrhea. The incidence of hypogonadotropic-hypogonadism presenting as primary amenorrhea was similar to earlier report by Kwon et al⁷ However CDGP patients presenting with primary amenorrhea was lower which could be due to lower number of patients presenting in the study period. Prolonged untreated hypothyroidism can also manifest with primary amenorrhea as found in our study. The incidence of AIS presenting as primary amenorrhea was similar to report by Kwon et al⁷ Kwon et al showed most common cause of primary amenorrhea was gonadal dysgenesis (28%), followed by MRKH syndrome (20%), CDGP (8.3%) and AIS (8.3%) respectively. A recent study by Klein and Poth.⁸ reported that primary amenorrhea is the result of primary ovarian insufficiency (e.g.; Turner syndrome) or anatomic abnormalities (e.g.- Mullerian agenesis). Another study by Reindollar et al⁹ showed the most common cause of primary

amenorrhea in American population was gonadal dysgenesis.

The treatment of amenorrhea requires first determining its cause, so a thorough history and physical examination, accompanied by imaging studies and measurement of hormone levels are important to narrow the differential diagnosis. Treatment goals include the prevention of complications such as osteoporosis and endometrial hyperplasia from the associated abnormal hormonal levels and preservation of fertility.^{1,10}

CONCLUSION

In concordance with other studies, Turner syndrome and Mullerian agenesis are the commonest cause of primary amenorrhea in our study. The relatively later age of presentation as compared to other reports may reflect lack of awareness about primary amenorrhea prevailing in this region. In contrast to certain western reports primary amenorrhea rather than short stature remains the commonest cause for seeking medical evaluation in patients with Turner syndrome. In cases of primary amenorrhea treatment should be started immediately following the diagnosis, with the primary therapeutic goal being to facilitate normal secondary sexual development. Thus these patients must be managed in individualized manner to obtain maximum therapeutic benefit.

ABBREVIATIONS

MRKH-Mayer- Rokitansky-Kuster- Hauser syndrome, AIS- Androgen Insensitivity syndrome, CDGP- Constitutional Delay in Growth and Puberty.

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