VOLUME-8, ISSUE-6, JUNE-2019 • PRINT ISSN No. 2277 - 8160

Original Research Paper

Endocrinology

ETIOLOGICAL PROFILE OF PRIMARY AMENORRHEA IN KASHMIR VALLEY

Zhahid Hassan	DM Endocrinology
Rahat Abbas*	MD gynecology *Corresponding Author
Farhat Abbas	MD pathology
Mohsin Gayas	MBBS

ABSTRACT

Background: Primary amenorrhoea is defined as absence of menstruation by the age of 14 in absence of secondary sexual characteristics and by age 16 regardless of the presence or absence of secondary sexual characteristics. 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.

Aims and objectives: To determine etiologic causes of primary amenorrhea in kashmeri population.

Materials and methods: This is a prospective and observational study conducted in department of endocrinology at skims from jan 2015 to jan 2017.Cases were analysed according to clinical profile, development of secondary sexual characteristics, physical examination, relevant biochemical, hormonal and radiological investigations as indicated.

Results: The three most common causes of primary amenorrhea were hypergonadotropic hypogonadism 40.50%, hypogonadotropic hypogonadism 34.17% and mullerian agenesis 12.65%.Turner syndrome and gonadal dysgenesis were common in hypergonadotropic hypogonadism and idiopathic gonadotropin deficiency and constitutional delay in growth and development were common in hypogonadotropic hypogonadism .

Conclusion: Prompt reporting and awareness of available treatment options based on the etiology can make a huge difference in this often underreported disorder

KEYWORDS :

INTRODUCTION:

Amenorrhea is absence of menses in women of reproductive age. 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 (PA) is defined as the absence of menarche by the age of 14 without the development of secondary sexual features or lack of menstruation by the age of 16 despite the existence of secondary sexual features.[3]This is a rare disorder occurring in less than one percent of female population.[4] According to World Health Organiz ation estimates, amenorrhea stands as sixth largest major cause of female infertility and affects 2.5% of all women in the child bearing age[5].About 2.5% of adolescent girls present with primary amenorrhea[6]. Normal menstrual cycles requires normal function of the hypothalamus, pituitary, ovaries and out flow tract. Failure of menses can be due to a problem at any of these levels [7, 8]. Although primary amenorrhoea has long been recognized and the literature on this problem is profuse, there are not many studies on large numbers of patients, but the incidence of the diseases that cause this problem may vary from area to area due to different racial groups of patients. Since there are few large series on this topic from India, the present study was undertaken to determine the incidence of etiologic factors responsible for primary amenorrhoea in Kashmir North India at tertiary care centre on the basis of clinical examination and laboratory investigation.

MATERIALS AND METHODS:

This is a prospective and observational study conducted in department of endocrinology at skims from jan 2015 to jan 2017. All patients with primary amenorrhea attending skims endocrine opd were included in study. A careful complete history and physical examination were taken. The height, weight, blood pressure were measured and all patients were examined for hirsutism and other signs of virilization. The extent of breast, axillary hair and pubic hair development were determined by an endocrinologist. The thyroid gland and breasts were examined for goiter and galactorrhea. When history and physical examination were completed and systemic chronic disease were excluded, baseline FSH, LH and estradiol were measured in all patients to determine whether the patient had hypogonadotropic (FSH↓, LH↓) or hypergonadotropic hypogonadisem (FSH↓, Lh↓). In hypergonadotropic patients with short stature with or without other stigmata of Turner's syndrome, chromosomal analysis was performed. Seventeen hydroxyprogesterone (17 OHP) was measured in the morning and in patients especially with evidences of androgen excess (hirsutism, acne). 17 OHP levels was greater than or equal to 200 ng/dl (6 nmol/l). ACTH stimulation test was performed and baseline 17 OHP and cortisol and stimulated 17 OHP and cortisol after 30 minutes 250 microgram short acting ACTH (Cosyntropin) IV bolus injection were measured for screening of 21-OH deficient NCCAH. In hypogonadotropic patients with or without galactorrhea and goiter, prolactin, T4 and TSH assays were performed. In addition pelvic USG and CT Scan or MRI of the brain was also performed. The data was analysed using standard statistical methods. The graphs and tables were generated using Microsoft excel 2010 software.

RESULTS:

A total of 79 patients were evaluated in the study period. The mean age of presentation of patients with primary amenorrhea was 20.01 ± 4.08 years. Most of the patients presented between 10-20 years of age (63.29%, N= 50), followed by age group 21- 30 years (36.3%, N=29) (Figure 1

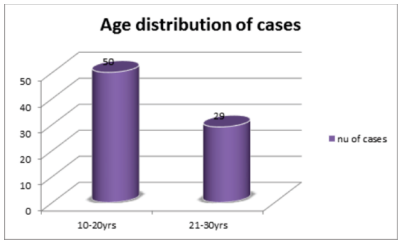

Fig 1

Among 79 female patients who were studied, 32 cases (40.50%) had hypergonadotropic hypogonadism.27 cases (34.17%) had hypogonadotropic hypogonadism and 10cases(12.65%) had mullerian agenesis.fig 2

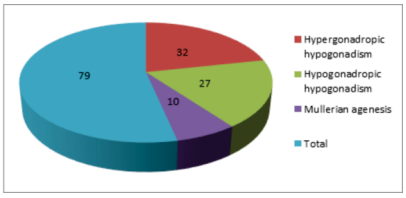

Fig 2

In 32 cases of hypergonadotropic hypogonadism 9 cases (28.12%)were turner syndrome, 8 cases (25%) were of each congenital adrenal hyperplasia and gonadal dysgenesis,5 cases (15.6%) were of complete androgen insensitivity syndrome and 2 cases(6.2%) were of polycystic ovarian syndrome Table 1 and fig 3. Among 27 cases of hypogonadotropic hypogonadism 7 cases (25.92%) were of idiopathic gonadotropin deficiency 6 cases (20.68%) were constitutional delay in growth and development, (CDGD),5 cases (17.24%) were hypopituitarism , 3 cases (10.3%) were hyperprolactinemia, 2 cases (6.8%) were kallman syndrome and 4 cases (13.79%) were of systemic diseases which included 2 cases of tuberculosis,1 case of each chronic kidney disease and celiac disease. 10 cases (12.65%) were of mullerian agenesis. Table 2 and fig 4

Table 1. Etiologies of hypergonadotropic hypogonadism in 32 female patients

Etiology	Number of cases	Percentage
Turner syndrome	9	28.12
CAH	8	25
Gonadal dysgenesis	8	25
CIS	5	15.6
PCOS	2	6.2
Total	32	100

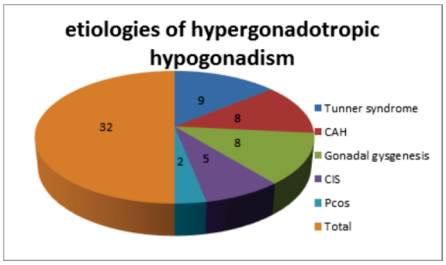

Fig 3

Table 2. Etiologies of hypogonadotropic hypogonadism in 27 female patients

Etiology	Number of cases	Percentage
CDGD	6	22.22
Idiopathic gonadotropin deficiency	7	25.92
Kallman syndrome	2	7.4
Hypopituitarism	5	18.51
hyperprolactinemia	3	11.11
Systemic diseases	4	14.81
Total	27	100

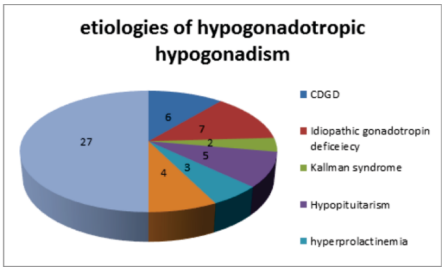

Fig 4

DISCUSSION:

Primary amenorrhea refers to a lack of menstruation by age 16 years in the presence of breast development or by age 14 years in the absence of breast development.[7-10].Amenorrhoea is a symptom that reflects some underlying disease anywhere in the hypothalamic-pituitary-ovarian-uterine axis. There are different causes of primary amen orrhoea. It includes anomalies of mullerian development, gonadal dysgenesis, constitutional delayed puberty, tuberculosis, CNS tumors, idiopathic etc[11]. Previous studies have been reported from all parts of the world indicating the frequency of various etiologies, cytogenetic abnormalities in cases of primary amenorrhoea. Gonadal dysfunction has been considered as the commonest factor for primary amenorrhoea worldwide followed by pituitary/hypothalamic disorder and outflow tract anomalies [12]. Literature shows greater prevalence of gonadal dysfunction leading to primary amenorrhoea in western countries while that of outflow tract anomalies in Asian- African countries. Most of the studies from United States have mentioned gonadal dysgenesis as the most common cause of amenorrhoea awhile a large study from Thailand of 295 cases has shown Mullerian anomaly as the commonest cause in Thai population[12-15]

In our study turner syndrome and gonadal dysgenesis were common causes of primary amenorrhea in patients with hypergonadotropic hypogonadism and idiopathic gonadotropin deficiency and constitutional delay of puberty were common causes in patients with hypogonadtropic hypogonadism. Mullerian agenesis being most common cause in many indian studies was seen in only 12.65% of cases. The proposed reason for this difference might be the environmental and racial or genetic influence 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 MPHD (7.14%). In our study, the mean age of presentation was 20.21 ± 4.08 years. Gonadal dysgenesiswas noted in 25 % of our cases of primary amenorrhoea which was comparable to 29.05 % in the study by Quorrata et al [16] & 35.3 % in the study by Prasong et al, [17]. Reindollaret al. in his study showed that the most common cause of primary amenorrhoea in the American population was gonadal dysgenesis (48.5%) [13].

Being a major concern in pubertal girls, primary amenorrhea affects physical, mental, psychological and social life of the patient 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. [1,18].

CONCLUSION :

The etiologic causes of primary amenorrhoea in our study are different from other indian studies. Racial and environmental differences, facilities for diagnostic tools may contribute to these differences. As diagnosis based on inadequate data may be misleading, both clinical examinations & laboratory investigations have to be completed before final diagnosis of primary amenorrhoeais established. Early recognition of the definite etiology and institution of the appropriate treatment will minimize late complications.

REFERENCES

1) Heiman DL. Amenorrhea. Prim Care 2009;36(1):1-17.
2) Master-Hunter T, Heiman DL. Amenorrhea: evaluation and treatment. Am Fam Physician 2006;73(8):1374- 1382
3) Lippincott Williams and Wilkins; 2011. Amenorrhea; 435-493. Speroff L, Marc A. Fritz. In: Clinical Gynecologic Endocrinology and Infertility. 8th ed. USA:
4) Macdonald G. Harrison's internal medicine. In: Fauci AS, Kasper DL, Longo DL, et al, eds. 17th edn. Internal Medicine Journal 2008;38(12):932.
5) Dutta UR, Ponnala R, Pidugu VK, Dalal AB. Chromosomal abnormalities inamenorrhea: a retrospective study and review of 637 patients in south India.Arch Iran Med 2013;16(5):267e70.
6) Wachtell SS. The genetics of intrasexuality: clinical and theoretic perspective.Obstet Gynecol 1979;54:671e83
7) Carr BR. Disorders of the ovaries and Female reproductive system. Williams text book of endocrinology, 9th edition, Philadelphia; W.B. Saunders company 1998; 783-95.
8) Rosenfield RL. Hypogonadism. Pediatric Endocrinology, Mark A. Sperling (ed), W.B. Saunders company, 1996; 361-369.
9) Goldfien A, Monroe SE. Disorders of ovarian and menstrual function. Francis S.Greenspan, Gordon J. Strewler, Basic and clinical endocrinology, Fifth edition, Appleton and lange, 1997; 453-463.
10) Wilson MD. Amenorrhea. Oskies pediatrics, Third edition, J.B.Lippincott company, 1999; 539-542.
11) Speroff L, Glass RH, Kase NG, editors. Clinical gynecologic Endocrinology andinfertility. 6th ed. USA: Lippincott Williams and Wilkins; 1999. Amenorrhea;pp. 421-76
12) Schorge JO, Schaffer JI, Halvorson LM, Hoffman BL, Bradshaw KD,Cunningham FG. Amenorrhea. In: Schorge JO, Schaffer JI, editors. Williamsgynecology. New York, NY: McGraw Hill; 2008. p. 1112-28.
13) Reindollar RH, Tho SPT, McDonough PG. Delayed puberty: an update study of326 patients. Trans Am Gynecol Obstet Soc 1989;8:146-62
14) Reindollar RH, Byrd JR, McDonough PG. Delayed sexual development: a studyof 252 patients. Am J Obstet Gynecol 1981;140:371-80.
15) Tanmahasamut P, Rattanachaiyanont M, Dangrat C, Indhavivadhana S,Angsuwattana S, Techatraisak K. Causes of primary amenorrhea: a report of295 cases in Thailand. J Obstet Gynaecol Res 2012;38:297-301
16) QuorrataEynulForhad, SumayyaTasnim ,Anowara Begum. Primary Amenorrhoea - Analysis of 44 cases; Bangladesh J ObstetGynaecol, 2008; Vol. 23(2) : 46-50.
17) PrasongTanmahasamut, ManeeRattanachaiyanont, ChongdeeDangrat, SuchadaIndhavivadhana, Surasak Angsuwattana and KitiratTechatraisak. Causes of primary amenorrhea: A report of 295 casesin Thailand; J. Obstet. Gynaecol. Res. Vol. 38, No. 1: 297–301,
18) Reichman DE, Laufer MR. Congenital uterine anomalies affecting reproduction. Best Pract Res Clin Obstet Gynaecol 2010;24(2):193-208.