Original Article

Frequency of Primary Amenorrhea and its Management at Tertiary Level Hospital

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Abstract

Objective: The goal of this study was to determine the frequency of primary amenorrhea and to identify etiological factors and outcomes.
Methodology: A descriptive case series study was conducted in Department of Obstetrics and Gynecology (Unit-I) Federal Govt Polyclinic Islamabad, from September 2016 to August 2018. Patients with secondary amenorrhea were not included in study. Only patients with primary amenorrhea were included. The data obtained through the history, examination, and investigation was entered into Performa. SPSS 10.0 was used to analyze the data.
Results: Total number of patients enrolled in outpatient gynecology was 7854. Twenty one patients presented with primary amenorrhea. The prevalence was 0.27%in our study. Mullerian anomalies were seen in 10 patients (47.6%). The outcome was good in all patients with cryptomenorhea. Premature ovarian failure was seen in 07 patients (33%). Hypothalamic causes were seen in 03 patients (14.3%). 01 patient had polycystic ovarian disease (4.7%). One patient remained undiagnosed.
Conclusion: Primary amenorrhea is a stressful condition, must be dealt with great sensitivity. Thoughtful counselling should be provided to all patients and family members. Primary amenorrhea is associated with long-term risks ,and decreased quality of life. Fear of exposure to the defect and poor outcome regarding future fertility was a major reason for reluctance to investigation and follow up. Marital issues must be focused on clearly.
Key words: Primary amenorrhea. Frequency. Causes. Follow up. Outcome.

Cite this article as: Israr N, Israr SN, Bashir L, Akhtar Z.Frequency of Primary Amenorrhea and its Management at Tertiary Level Hospital. J Soc Obstet Gynaecol Pak. 2022; 12(3):241-245.

Introduction

Primary amenorrhea is a symptom with an extensive number of underlying causes. Amenorrhea means absence of menstrual cycles, it is of two type's primary, and secondary amenorrhea .Primary amenorrhea is defined absence of menses by 14 years of age in the absence of growth or development of secondary sexual characteristics. In contrast cessation of previous regular periods for more than six months is secondary amenorrhea.[1] Anatomical defects, increased levels of the hormone follicle-stimulating hormone (FSH), hyperprolactinemia, hypothalamic amenorrhea, or polycystic ovary syndrome(PCOS) are responsible for the majority of primary amenorrhea cases. [2] Amenorrhea affects 2-5% of all women in reproductive age.[3] It is the sixth most common significant cause of female infertility.[4] Amenorrhea is divided into three categories by the World Health Organization. Women who do not exhibit endogenous estrogen production, have normal or low levels of follicle-stimulating hormone (FSH), normal levels of prolactin, and no signs of lesions in the hypothalamic-pituitary region are included in WHO group 1. WHO group II females with normal hormone level and the capability to produce estrogen. Women in WHO group III have higher serum hormone level, which indicate gonadal insufficiency or failure.[5]

If regular menstruation has not started within two years of the start of otherwise normal adolescence, Shearman suggested ruling out congenital absence of the

Authorship Contribution: [1,3]Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, Final approval of the version to be published, [4]Drafting the work or revising it critically for important intellectual content, participated in the acquisition and data analysis, [2,4]Active participation in active methodology.

Funding Source: none
Conflict of Interest: none

Received: Feb 15, 2022
Accepted: Aug 21, 2022

uterus/vagina if it has not yet been clinically detected. [6] This study will help to know frequency of cases, their causes, and can guide to manage primary amenorrhea. Ross suggested that primary amenorrhea should be explored If sexual infantilism lasts until the age of 16 or if, despite of the normality of secondary sexual features, menstruation has not started by the age of 18. [7]

Pubertal change typically occurs over a period of three-years and can be measured using Tanner staging.[8] A complex interaction of hypothalamic-pituitary-ovarian axis and the outflow tract (uterus, cervix and vagina) is required for normal menstrual cycle to take place. Amenorrhea can result from any interruption in this axis.[9] A primary amenorrhea case needs to be carefully examined because it affects the patient's physical and mental health. To avoid long-term health and social impacts, early diagnosis and early management are necessary.

Methodology

This study was conducted in the Federal Govt. Polyclinic (PGMI) Islamabad's unit-1 of obstetrics and gynaecology over the period of two years, from September 2016 to August 2018. All patients who met the inclusion requirements were included. The confidentiality of the information collected from patients and their families were assured. Patients with secondary amenorrhea were excluded .The evaluation of amenorrhea begins with through medical history and physical examination

Physical examination included examination of height, weight, built, BMI, nutritional status, secondary sexual characteristics (breast and areolar development, pubic and axillary hair) acne, hirsutism and glactorhea. Pelvic or rectal examination was done to see the external genitalia, imperforate hymen, absent or blind ending vagina, presence and absence of uterus and cervix.

A complete blood count and comprehensive panel of tests advised for each patient based on provisional diagnosis derived from history and examination. Diagnostic Laparoscopy was done in selected patients. Pregnancy test was done wherever necessary. Pelvic ultrasonography (Trans abdominal or transvaginal) was done for all patients.

Results

Total number of patients seen in gynecology department, Unit-1 were 7854. Primary amenorrhea was diagnosed in 21 patients with prevalence of 0.27%. In our study enrolled patients age was 13 to 32 years. The height of patients were not clinically different among all . Breast were developed in 9(42.9%) and infantile in remaining patients, while pubic and axillary hairs were well developed in 12 (54.7%) and were scanty in 9 patients (42.9%). External genitalia were normal in 11 cases and poorly estrogenised in other patient's, ambiguous genitalia were not seen in any patient.

Kariotyping was done in 09 patients, as it is an expensive test so some patients were reluctant. Hormonal assay was done in in 12 (57.1%) FSH was raised in 7 patients, these seven patients were real sisters from same family, and ovarian biopsy was not done in them. In addition, FSH was low in 03(14.3%) patients and normal in 2(9.5%) patients, one was diagnosed as polycystic ovarian disease on pelvic ultrasound and physical examination. In 21 patients of primary amenorrhea only one patient was undiagnosed which turned into constitutional delayed puberty. She had spontaneous periods after one and half year. In our study, 03(14.3%) patients were married. Three patients were treated surgically for cryptomenorhea caused by imperforate hymen. One patient had absent cervix with non-communicating vagina, Abdominal hysterectomy was done with preservation of ovaries. Two patients had a double uterus with non-communicating vagina, one of them had abdominal hysterectomy and other had successful communication of vagina followed by regular menses after surgery. According to underlying cause of primary amenorrhea, different treatment options were

Table I: Sonographic and Other Paraclinical Finding.

Diagnosis	No	Son graphic finding		Karyotype	FSH-LH	Treatment
		Uterus	Ovaries			
Rokitiansky syndrome(MRKH)	3	Absent or rudimentary	Normal	xx	ND	Surgical Correction
Vaginal septa	3	Hematormetra	Normal	xx	Normal	Surgical
Absent Cervix	1	Hematormetra	Normal	ND	ND	Surgical
Uterus with Horn, Non communicating vagina	1	Double uterus	Normal	xx	ND	Reassurance
Premature ovarian failure	7	Hypo plastic	Streak	xx	Raised	Hormonal support
Hypothalamic	2	Hypo plastic	Normal	xx	Low	Hormone support
Polycystic ovarian disease	1	Normal	Polycystic	ND	ND	Medical
Undiagnosed	1	Normal	Normal	xx	ND	Hormone support

Table II: Results of enrolled patients.	
Prevalence or Primary amenorrhea	0.27%
Age of patients	13-28 years
Married	3(14.3%)
Karyotype	19(90.5%)
Hormonal Assay	12(57.1%)
Laparoscopy	8(38.1%)
Mullerian Anomaly	10(47.6%)
Premature Ovarian Failure	7(33%)
Hypothalamic	3(14.31)
Polycystic Ovary	1(4.7%)
Undiagnosed (constitutional delayed puberty)	1(4.7%)

advised, like healthy lifestyle, healthy diet, calcium and vitamin D intake, anti-depressant therapy, and stress management.

Table III: Distribution of cases by age. (n=21)		
Age in years	**No of patients**	**Percentage (%)**
10-15	2	9.5%
16-20	8	38.1%
21 -26	7	33.3%
27-32	4	19.0%

Because primary amenorrhea can have a wide range of etiologies, patients' education must be addressed. They should have follow up with a physician on a frequent basis. Treatment options for infertility like in vitro fertilization with egg donation, Adoption, selective marriages were discussed. Support groups were encouraged.

Discussion

Primary amenorrhea poses a diagnostic dilemma. These patients present with specific sign and symptoms which points to words underlying etiology. It is really upsetting for patients and their families. Primary amenorrhea is associated with social, psychosexual, infertility, osteoporosis, and genital atrophy problems. Mostly it is diagnosed in young patients so should be dealt with extreme care, and needs a multidisciplinary team. Evaluation of primary amenorrhea begins with detailed history and examination and institute appropriate investigation. The important thing is to identify the presence or absence of secondary sex characteristics. The Tanner scale is used to stage pubertal growth. The absence of secondary sexual characteristic indicates that patient has never been exposed to estrogen. Either normal ovarian oestrogen production or peripheral androgen to oestrogen conversion imply normal breast growth. Because it is unlikely that peripheral conversion will result in full breast development, that's why the evaluation of secondary sexual is significant in primary amenorrhea.[10] Thyroid function test and prolactin should also be performed to rule out hypothyroidism and hyperprolactinemia as cause of amenorrhea. Both hypothyroidism and hyperthyroidism can be associated with amenorrhea. In our setup,among 7854 individuals primary amenorrhea frequency was 0.27%. In contrast, a study carried out in 2004 at the Dow Medical College and Civil Hospital Karachi found that among 19,900 cases, the frequency of primary amenorrhea was 0.065%.[10] Imperforate hymen (21.05%) was the most common cause in her study. This was comparable to a study conducted in March 2003 at King Edward Medical College by Farhat Iqbal, in which they discovered 19.3% of cases of imperforate hymen.[11] In our study 03 patients had imperforate hymen with cryptomenorhea and surgical correction was done in them.

In our setup and society getting married and future fertility is considered big markers of success for females, so diagnosis of primary amenorrhea to them was quite disturbing. In this study, the three most common causes of primary amenorrhea were mullerian anomalies, premature ovarian failure, and hypogonadotrophic hypoganadism respectively. Similarly, Rao k and Pillian N's study in India and R Attandachaiyanont's study in Thailand discovered that mullirian agenesis is the most common cause.[12] The results of this study demonstrated that the diagnosis of primary amenorrhea can be made with the help of diagnostic tools like sonography.[13]

Trans-abdominal ultrasonography of the pelvis can be the imaging method of choice for patients presenting with primary amenorrhea and in guiding us through further work-up.[14] Trans -perianal or trans labial ultrasound has been proposed to assist in determining the causes of primary amenorrhea, when adequate vaginal access is not possible.[15] While MRI is increasingly utilized to examine the uterus and cervix, it has taken over as the preferred imaging modality for the diagnosis of congenital uterine anomalies.[16]

We found some drawbacks in our study, like many patients were not willing for karyotyping due to its cost and it is not available in every setup. Bec. Karyotyping is one of the fundamental investigation in the evaluation of primary amenorrhea. Abnormal karyotypes were un-common in our patients, and our karyotyping method did not rule out the possibility of minor structural abnormalities. It was done in 09 patients of our study and all were normal while others refused for it. It was found abnormal in 10.52% patients according to the study conducted by Rizwan et al[17] agrees with Rajanjam's findings, in which he discovered chromosomal abnormalities in 34.57% of patients.[18]

In our study, there were 10 patients (47.6%) who had mullerian anomalies; three of these patients had Mayor Rokistansky Kuster Hauser (MRKH) syndrome, which is described by primary amenorrhea, well-developed secondary sexual characteristics, female external genetalia, blind vagina, an absence or rudimentary uterus, and 46XX chromosomes. In contrast, Parichi et alstudy's found that MRKH syndrome was the most prevalent aetiology, almost 58% of all cases in their series.[19] Roa K mentioned in his study that majority of these are sporadic[20], but in some cases genetics familial tendency has been described.[21] A non-functional uterus with uterovaginal agenisis (Mayer Rokitansky- Kuster-Hauser Syndrome) is one of the most common causes of primary amenorrhea among congenital anomalies of the female genital tract.[22]

Premature ovarian failure is defined as the cessation of ovarian function, with raised basal levels of Follicle-stimulating hormone (FSH), luteinizing hormone (LH) and decreased level of estrogen of the menopausal range, before the age of 40 years. The mortality rate from cardiovascular disease, stroke, and osteoporosis increases by double with age, making POF a significant endocrine illness.[23] About 1% of women suffer from premature ovarian failure. Infertility due to insufficient ovulation and hypo-estrogenism are the main issues. Infections, autoimmune and enzymatic disorders, genetic predisposition, iatrogenic causes, and endocrine disorders are some of the potential causes of POF.[24] Premature ovarian failure is a devastating diagnosis for reproductive – aged women. In our study, seven patients were diagnosed with premature ovarian failure, and they are real sisters. The family had lot of problems with their management. Rizwan N in her study among 19 patients did not diagnose premature ovarian failure as a cause of primary amenorrhea.[17] In other investigations, there have been few reports of primary amenorrhea caused by early ovarian failure.[25] There were three cases of hypogonadothrophic hypogonadism. Jabeen S also reported such cases in her study.[26] The prognosis in term of fertility outcome is not clearly established. However, these techniques are so expensive that only a few can afford. In some studies, oogenesis has been successfully restored in the ovaries, but ovarian follicles have neither matured nor produced egg cells, and further research is needed.[27] One patient in our study had poly cystic ovaries and after 18 months had regular cycles with weight reduction and treatment. There was one case (4.7%) which was quite challenging for us, this patient all investigation were normal and she did not show any response to combined oral contraceptive pills for 3 months. We labeled this case as receptor deficiency, Jabeen S[25] and Tavasoli et al[27] reported such cases. The cause could be endometrial hypoplasia as endometrial thickness was less than 3 mm.

We have reported this study to highlight prevalence and management of primary amenorrhea at a tertiary center. The present study had few limitations, as it was a single center study at tertiary hospital so study population was of that hospital only. Aim was to develop sensitive approach towards their management after diagnosis.

Conclusion

The stressful situation of primary amenorrhea creates a difficult diagnostic challenge. Specific indications and symptoms that these patients exhibit indicate to an underlying cause. Thought full, SYMPATHATIC counselling must be done all patients and family members. Long-term health issues must be discussed in detail. It is associated with long-term risks and decreased quality of life. Fear of being exposed to a defect and having a poor outcome in terms of future fertility was a major reason for the reluctance to investigate and follow up. Openly share information, and coordinate in educating them. Martial issues, fertility options must be discussed, like in vitro fertilization with egg donation, adoption, and selective marriage. Support groups to be encouraged.

References

1. Lord M, Sahni M, StatPearls[internet}. StatPearls Publishing; Treasure Island(FL): May 3,2022.Secondary Amenorrhea
2. Klein DA,Paradise SL, Reeder RM. Amenorrhea: A Systemic Approach to Diagnosis andManagment. Am Fam Physician. 2019;100(1): 39-48.
3. U R Dutta, R. Ponnala VK. Pidugu AB. Chromosomal abnormalities in amenorrhea: a retrospective study and review of 637 patients in south India Arch Iran Med.2013; 16 (5): 267-270.
4. SS Wachtell. The genetics of intersexuality: clinical and theoretic perspective Obstet Gynecol.1979;54:671-683.
5. Wei HL, Lu S, Wang XL, Li JW, Cui YP, Yao YS. Hydroxylase deficiency with severe hypertension as the intial symptom in a child]. Zhongguo Dang Dai Er Ke Za Zhi. 2018; 20(8):675-679.
6. Shearman RP, Roberts J. The embryology and endocrinology of primary amenorrhea: a study of one hundred and forty patients. Clin. Reprod Fert. 1982; 1: 117-30
7. Ross G T. Diagnosis and management of primary amenorrhea, secondary amenorrhea and dysfunctional uterine bleeding. Endocrinol. 1979; 10: 1419-33.
8. Marshall WA, Tanner JM. Variation in patterns of pubertal changes in girls. Arch Dis Child. 1969; 44: 291-303.

9. Speroff L. Glass RH, Kase NG. Normal and abnormal sexual development in Clinicalgyneacolgic and infertality. 6th ed. Baltimore, Md: Lippincott William7 Wilkins. 1999:339-79.
10. Ghazi A, Jabbar S. Frequency and causes of primary amrnorrhoea at Civil Hospital Karachi. Pak J Surg. 2004; 20(1):35-7.
11. Iqbal F, Naheed I. primary amenorrhea- a review of 26 cases. Ann King Edward Med Coll. 2003; 9(10: 21-3
12. Rao k, Pillii N V. Primary amenorrhea (analysis of 40 cases). J Inevakdian Medical Association. 1991; 89:42-3.
13. Rattanachaiyanont M, Kurra thikom S, Angyowattana s, Techatraisak K, Mekmahan O, Karavagul C, et al. Primary amenorrhea: a retrospective study at Siriraj Hospital: J Med Assoc Thai. 1997 Oct;80(10) :619-25.
14. Spevak MR, Cohen HL, Ultrasonography of adolescent Female pelvis. Ultrasound Q.; 18:275-88.
15. Meyer WR, McCoy MC, Fritz MA. Combined abdominal-perineal sonography to assist in diagnosis of transverse vaginal septum. Obstet Gynecol. 1995; 85(5 pt 2):882-4.
16. Brown MA, Rachel A, Huck K, Reinhold C, Semelka R. Uterus and cervix. In: Semelka RC. Abdominal Pelvic MRI. New Jersey: Wiley-Liss Inc; 2006.
17. Rizwan N, Abbasi Rm. Frequency of primary amenorrhea and the outcome of treatment at Liaqat University Hospital. J Liaq Univ Med Health Sci.2008; 110-3.
18. Rajangam S, Nanjappa l. Cytogenetic studies in amenorrhea. Saudi Med J. 2007; 28(2): 187-92.
19. Parik RM, Nakum K, Kadikar GK, Gokhle AV. Mullerian anomalies a cause of primary amenorrhea. Int J Reprod Contracept Obstet Gynaecol. 2013; 2 (3); 393-7.
20. Roa K, Pillai NV.Primary amenorrhea: analysis of 48 cases, J Indian Med Assoc. 1998; 96(4):119-20.
21. Tiker F Yildrim SV, Baruta o, Bagis T, Familial mullerian agenesis. Turk J Pediatr. 2000; 42(4): 322-4.
22. Morgan T, Turner syndrome; diagnosis and management. Am Fam Physician. 2007 .76(3):405-10.
23. Svetlana V. Aetiology of premature ovarian failure, Menopause International. 2009; 15:72-5.Kovanci E, Schutt AK. Premature ovarian failure;clinical presentation and treatment. Obstet Gynecol Clin North Am.2015;42:153-161.
24. Coulam CB, Adamson DB, Annegers Jf, et al, Incidence of premature ovarian failure, Obstet Gynecol, 1986;67;604.
25. Jabeen S, Races M, Nisar M. Frequency of different causes of primary amenorrhea at tertiary level hospital. J Ayub Med Coll Abbottabad. 2018; 30(3):60-3.
26. Bukovsky A.Can ovarian infertality be treated with bone marrowor ovary derived germ cells? Reprod Biol Endocrinol. 2005;3:36.
27. Tavasoli F, Hafizi L, Aalami M. Pelvic endometriosis in a patient with primary amenorrhea. J Reprod Infertil. 2009;10(2):145-50.