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# ROLE OF IMAGING IN PRIMARY AMENORRHEA- A PROSPECTIVE STUDY.

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**Abstract**

Background: Amenorrhea is the sixth major cause of female infertility affecting 2–5% of women in reproductive age. Primary amenorrhea affects 2–5% of adolescent girls. Early diagnosis and treatment is necessary to prevent complications and social consequences. Imaging plays a vital role in etiology of primary amenorrhea. Ultrasound is the first line investigation while Magnetic resonance imaging is important for accurate diagnosis and surgical planning.

Aim and Objective: Determine etiology of primary amenorrhea in Kashmiri tertiary care centre and assess role of imaging (USG, CT, MRI) in determining its etiology.

Materials and Methods: This was a hospital based prospective study done by departments of Gynaecology and Obstetrics and Radiodiagnosis and Imaging done in SKIMS hospital from Febuary to December 2019. 46 adolescent girls with primary complain of primary amenorrhea visited hospital's out patient department.

Results: Eugonadism was the most common cause of primary amenorrhea in our study accounting for 60.8% cases followed by Hypogonadotropic hypogonadism in 28.2% cases and hypergonadotropic hypogonadism in 10.8% cases. Mayer-Rokitansky-Kuster-Hauser syndrome was the most common cause of primary amenorrhea accounting for 21.7% cases followed by constitutional delay in 17.3% cases and polycystic ovarian disease in 13% cases.

Radiological investigations primarily ultrasound and magnetic resonance imaging were directly or indirectly involved in diagnosing 65.5% cases of primary amenorrhea. Radiological Imaging was least useful in patients with constitutional delay.

Conclusion: Radiology should be the first referral department in primary amenorrhea patients. Imaging is helpful in identifying cause of primary amenorrhea in majority of patients. Other modalities like karyotyping, laboratory investigations, clinical examination etc are helpful as well in addition to imaging.

**Keywords:** Primary Amenorrhea, ultrasound(USG), Magnetic resonance Imaging(MRI), Computerized tomography(CT), Mayer-Rokitansky-Kuster-Hauser (MRKH).

## Introduction

Absence of menarche by 14 years of age in the absence of secondary sexual characteristics or absence of menses by 16 years in the presence of normal growth and secondary sexual characteristics is termed as primary amenorrhea [1]. Amenorrhea is the sixth major cause of female infertility affecting 2–5% of women in reproductive age [2]. Primary amenorrhea affects 2–5% of adolescent girls [3].Amenorrhea is a symptom not a disease and cause can be anywhere from hypothalamic-pituitary axis to uterus-ovary. Normal neuroendocrinological, embryological development and genetic makeup is essential for normal menstruation. Primary amenorrhea affects physical and psychological wellbeing of the patient. Early diagnosis and treatment is necessary to prevent complications and social consequences. On the basis of Gonadotropin and Estrogen levels there are three types of primary amenorrhea.

**Table 1:** Classification of primary amenorrhea on gonadotropin levels.

| Categories of Amenorrhea Based on Gonadotropin and Estrogen Levels | | | |
|---|---|---|---|
| Type of Hypogonadism | LH/FSH | Estrogen | Primary Defect |
| Hypergonadotropic | High | Low | Ovary |
| Hypogonadotropic | Low | Low | Hypothalamus/Pituitary |
| Eugonadotropic | Normal | Normal | Varied |

Decreased ovarian function (hypogonadism) may result either from a lack of stimulation by the gonadotropins (hypogonadotropic hypogonadism) or from primary failure of ovary (hypergonadotropichypogonadism). Several disorders are associated with relatively normal LH and FSH levels (eugonadotropic), however, appropriate cyclicity is lost.Numerous classification systems for the diagnosis of amenorrhea have been developed, and all have their

strengths and weaknesses. One system divides causes of amenorrhea into anatomic versus hormonal etiologies, with further division into congenital versus acquired disorders. The two main causes are mullerian anomalies and gonadal dysgenesis with different frequencies in different parts, some have shown anatomic abnormalities as the most common cause while others have reported gonadal failure as the commonest one[4], [5], [6], [7].

**Aim and Objective**:

1. Determine etiology of primary amenorrhea in tertiary care centre of Kashmir.
2. Role of imaging (Ultrasound, Computerized Tomography, Magnetic Resonance Imaging) in diagnosis cause of primary amenorrhea.

**Materials and methods**:

This was a hospital based prospective study done by departments of Gynaecology and Obstetrics and Radiodiagnosis and Imaging done in SKIMS maternity hospital from Febuary to December 2019 for a period of 11 months. 46 adolescent girls with primary complain of primary amenorrhea visited hospital's outpatient department. Study was approved by institutional ethical committee with informed consent from patients.

Complete physical examination included examination of height, weight, built, BMI (body mass index), presence of secondary sexual characters, development of breasts, local examination of external genitalia to rule out imperforate hymen. Examination of hairline, carrying angle of elbow etc. to rule out low hairline suggestive of Turner syndrome was also done.

Laboratory investigations: The initial workup included serum luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin, and thyroid-stimulating hormone(TSH) levels, serum free and total testosterone and dehydroepiandro steronesulphate, estradiol and 17-OHP. Complete and differential blood count, Mantoux test whenever needed was done whenever required.

Radiological investigations like transabdominal USG, MRI were done .Computerized Tomography was avoided as there was high radiation dose involved except in one case of adrenal tumor. Karyotyping was done in cases of primary gonadal failure and those with symptoms of androgen excess.

Inclusion Criteria: 1. Adolescent girls with primary amenorrhea.

Exclusion criteria: 1. Girls with previous operative history on genital system.

Girls receiving any sort of hormonal therapy.

**Statistical Analysis**:

Categorical values were presented with absolute and relative frequencies (%) and continuous values with mean.

**Results**:

Most of the patients were between 14 to 22 years of age with maximum number of patients (15 out of 46) having age of 16 years accounting for 32.6% cases (Table 1). Eugonadism was the most common cause of primary amenorrhea in our study accounting for 60.8% cases followed by Hypogonadotropic hypogonadism in 28.2% cases and hypergonadotropichypogonadism in 10.8% cases (Table 2). Mayer-Rokitansky-Kuster-Hauser (Figure 1) syndrome was the most common cause of primary amenorrhea accounting for 21.7% cases followed by constitutional delay in 17.3% cases and polycystic ovarian disease in 13% cases (Figure 2). Thyroid disease in form of hypothyroidism accounted for 10.8% cases.Pituitary adenoma either microadenoma or macroadenoma accounted for 10.8% cases. Vaginal septum and imperforate hymen accounted for 6.5% and 4.3% cases. Turner's syndrome and gonadal dysgenesis cases accounted for 4.3% cases. Androgen secreting Adrenal tumor, Prior radiation for leukemia and hypoplastic uterus accounted for 2.1% cases (Table 3).

Imaging in form of MRI was involved in diagnosing all cases of MRKH syndrome, pituitary adenomas (Figure 3 and 4), hypoplastic uterus (Figure 5), hematometra secondary to vaginal septum (Figure 6), one case with polycystic ovarian morphology and one case of gonadal dysgenesis. 2 cases of Imperforate hymen were diagnosed by local clinical examination. Ultrasound was used in patients with hypothyroidism and 3 out of 5 cases of hypothyroidism revealed thyroiditis (Figure 7) on USG. 4 out of 6 cases of polycystic ovarian disease had polycystic morphology on USG, and one patient of imperforate hymen had hematocolpos on USG. Contrast enhanced Computerized tomography was useful in diagnosing one case of androgen secreting adrenal tumor (Figure 8) in a patient with hirsutism. Radiological investigations were directly or indirectly involved in diagnosing 65.5% cases of primary amenorrhea. Radiological Imaging was least useful in patients with constitutional delay. Patients with Turner's syndrome and one case of gonadal dysgenesis were diagnosed by karyotyping and systemic examination. One patient with history of leukemia had received significant radiation dose which have presumed to be cause of premature ovarian failure. Girls with constitutional delay were diagnosed after excluding other causes of amenorrhea and positive family history.

**Table 1:**

| Age group | No. of patients |
|---|---|
| 10-13 years | 0 |
| 14-16 years | 22 |
| 17-19 years | 20 |
| 20-22 years | 4 |

**Table 2:** Age distribution of patients with primary amenorrhea

| Etiology | No. of patients | Percentage |
|---|---|---|
| Eugonadism | 28 | 60.80% |
| Hypogonadism | 13 | 28.20% |
| Hypergonadism | 5 | 10.80% |

**Table 3:** Distribution of patients on gonadotropin levels.

| Etiology | | No. of patients | Percentage |
|---|---|---|---|
| Eugonadism | MRKH | 10 | 21.70% |
| | PCOS | 6 | 13.00% |
| | Thyroid disease | 5 | 10.80% |
| | Vaginal septum | 3 | 6.50% |
| | Imperforate Hymen | 2 | 4.30% |
| | Adrenal tumor | 1 | 2.10% |
| | Hypoplastic uterus | 1 | 2.10% |
| Hypogonadotropic Hypogonadism | Constitutional delay | 8 | 17.30% |
| | Pituitary adenoma | 5 | 10.80% |
| Hypergonatropichypogonadism | Turners syndrome | 2 | 4.30% |
| | Gonadal dysgenesis | 2 | 4.30% |
| | Radiation | 1 | 2.10% |

**Table 4:** Frequency and percentageof etiology of Primary Amenorrhea

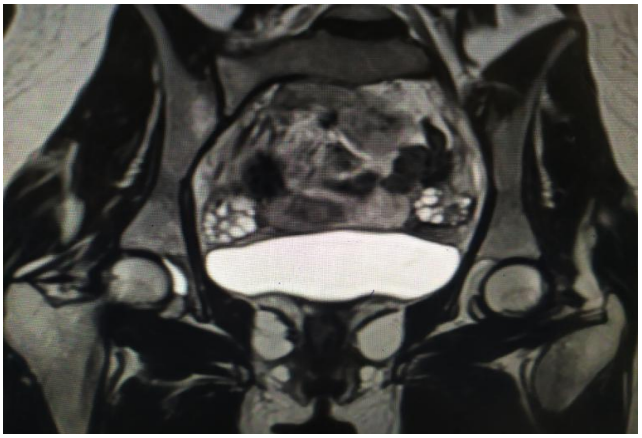

**Figure 1:** Coronal T2 weighted MR image showing absence of uterus with normal ovaries in MRKH syndrome.

**Figure 2:** Coronal T2 weighted MR image showing polycystic ovarian morphology.

**Figure 3:** Coronal T1 post contrast MR image revealing evidence of microadenoma.

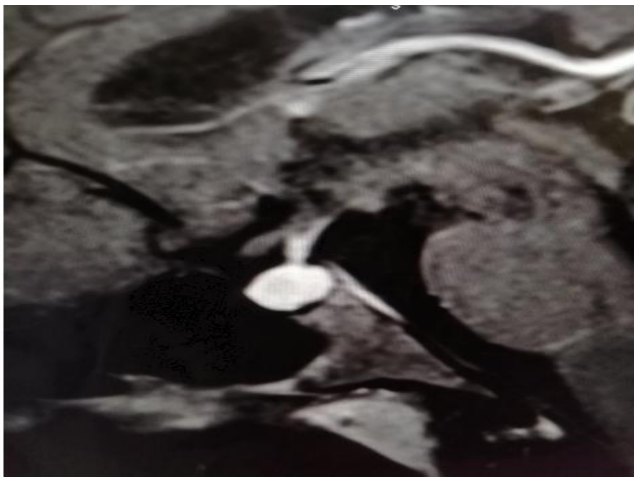

**Figure 4:** Sagittal post contrast T1weighted MR image revealing pituitary macroadenoma


**Figure 5:** Sagittal T2 weighted MR image showing hypoplastic uterus.

**Figure 6:** Axial T2 weighted Fat Saturated MR image showing hematometra in a case of transverse vaginal septum.

**Figure 7:** Ultrasound Image of thyroid showing enlargement and heterogeneous micocystic pattern in a case of thyroiditis.

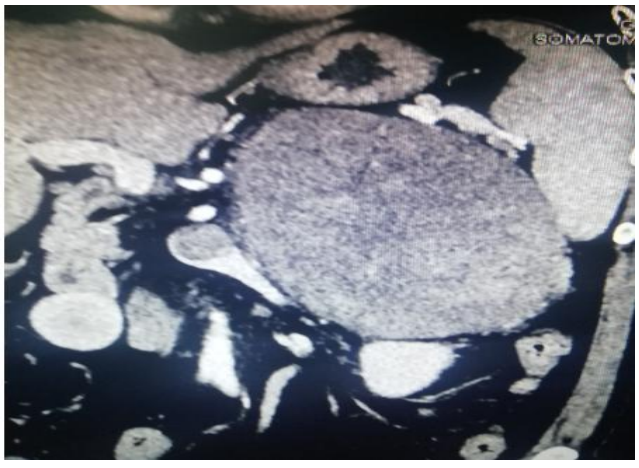

**Figure 8:** Contrast enhanced computerized tomography showing large left adrenal mass extending into left renal vein.

**Discussion**:

According to our study, Eugonadism was the most common cause of primary amenorrhoea in our study accounting for 60.8% cases followed by Hypogonadotropic hypogonadism in 28.2% cases and Hypergonadotropichy-pogonadism in 10.8% cases. Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome was the most common cause of primary amenorrhea in our study accounting for 21.7% cases followed by constitutional delay in 17.3% cases and polycystic ovarian disease in 13% cases. Thyroid disease in form of hypothyroidism accounted for 10.8% cases. MRKH results fromearly developmental failure of the müllerian ducts results in agenesis or hypoplasia of the proximal two-thirds of the vagina, cervix, and uterus. Clinical presentation occurs at puberty with primary amenorrhea[8]. Our study correlates with other studies conducted by ShubanaRasool et al [9] and Tushar M Shah [10] who reported Eugonadism and Meyer Rokitansky Kuster Hauser as the most common cause of primary amenorrhea. Rattanachaiyanont - M et al [11] in their study on 110 adolescent girls reported Mullerian agenesis in 39.6% cases. 32.6% patients in our study were 16 years old. This is in accordance to study done by Shubanarasool et al [9] in which 48.9% cases were in age group of 15-16 year. Low percentage of Hypergonadotropichypogonadism in our study is attributed to the fact that such patients tend to consult Endocrinologists before Gynaecologists for their short height. Grubb MR et al [12] in their study reported that 25-40% women with hypothyroidism are oligoamenorrheic or amenorrheic. Kashmir has low iodine content in soil accounting for high incidence of hypothyroidism in the valley. Adolescents in Kashmir should be evaluated for thyroid disorder if presenting with amenorrhea. High incidence of cases due to polycystic ovarian disease is due to changing life styles in form of increased intake of fast food and increased weight gain under western influence. The association of amenorrhea with bilateral polycystic ovaries and obesity was first described in 1935 by Stein and Leventhal [13]. Amenorrhea is also included in Rotterdam PCOS diagnostic criteria.

Radiological Imaging (MRI, USG, CT) were directly or indirectly involved in diagnosing 67% cases of primary amenorrhea. In our study all MRKH cases were diagnosed on MRI. MR imaging remains the preferred imaging modality for mullerian duct anomalies, as it exquisitely details both the uterine cavity and external contours and has shown excellent agreement with clinical MDA subtype diagnosis [14]. MR is the imaging of choice for diagnosing pituitary adenomas. Ultrasound is the modality of choice for diagnosing polycystic ovarian disease.

**Conclusion:**

Primary amenorrhea has multiple causes and Radiological imaging primarily ultrasound and Magnetic resonance is

capable of diagnosing more than two-third of them. Radiology should be the first referral department in primary amenorrhea patients. . Imaging is helpful in identifying cause of primary amenorrhea in majority of patients. Other modalities like karyotyping, laboratory investigations etc are helpful as well in addition to imaging.

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