

Etiology of Primary Amenorrhoea - A Study of 60 Cases in a Tertiary Care Centre, Western Rajasthan

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Abstract: Objective: To determine the prevalence of etiologic causes of primary amenorrhoea in Indian population. Material and method: A retrospective study was performed using 60 complete medical records of girls with primary amenorrhoea who attend unaid hospital, department of obstetrics and gynaecology, Dr. S. N. M. C from July 2019 to December 2019. Cases were analyzed according to clinical profile, development and development of secondary sexual characters, physical examination, pelvic examination, hormone profile, pelvic USG, MRI, cytogenetic study for karyotype.

1. Results

- 1) All the data of 60 cases of primary amenorrhoea are analysed on the basis of medical records available and diagnosis was made. Etiologies of 60 cases as per table no. 1 are shown.
- 2) The common causes of primary amenorrhoea were mullerian anomalies (47 cases, 78.33%), Gonadal dysgenesis (3 cases, 5%) & Hypogonadotropic hypogonadism (2cases, 3.33%) in decreasing order. There were 47 cases of mullerian anomalies with 30 cases of MRKH (Mayer-Rokitansky-Kuster-Hauser syndrome) and 17 cases of imperforate hymen. Pt with MRKH are treated with Mc Indoe's vaginoplasty and laparoscopic davydov vaginoplasty. Those cases who had partially canalized vagina did not require surgery. Pt with absent uterus were counselled regarding the future fertility option of surrogacy or adoption.
- 3) Cytogenetic study was available in three cases among these three cases one case had turner syndrome (46 x del (X) (q (13))). Pt with primary gonadal failure put on combined hormone therapy with estrogen and progesteron in last 12 days of month and supplements with calcium and vitamin D to prevent bone loss.
- 4) Androgen insensitivity syndrome (AIS, 46XY) was found in three cases. (5%) In these cases bilateral gonadectomy done.
- 5) There were two cases of Hyperprolactinemia. (3.33%) Pt with low level of pituitary gonadotropins, decreased drive to ovaries for production for estrogens and progesterone, require exogenous gonadotropins for ovarian stimulation. And most of these patients conceive with ovulation induction.
- 6) There were two cases of hypogonadotropic hypogonadism and three cases PCOD (Polycystic ovary syndrome). These Pt were given ovulation induction with gonadotropins.

2. Conclusion

Mullerian anomaly is the most prevalent etiologic factor leading to amenorrhoea followed by gonadal dysgenesis in our study. Racial, genetic, environmental factors play role in the cause of primary amenorrhoea. Absence of menstruation in women of reproductive age group. As per WHO amenorrhoea stands sixth largest major cause of female infertility. It is of two types;

- a) Primary amenorrhea

- b) Secondary amenorrhea

Primary amenorrhea: Absence of menstruation by the age of 15 years with normal development of secondary sexual characters (According to FOGSI). Absence of menarche by the age of 13 years along with the absence of development of secondary sexual characteristics. Prevalence about 0.3%.¹

Secondary amenorrhea: Cessation of previously regular menses for 3 months or previously irregular for 6 months. Prevalence about 3%.²

Study in India indicated that 11.1% of adolescent girls who presented with gynaecological complaints of menstrual disorders had primary amenorrhea. However the incidence of disease in women in general is less than 1%.

Pathophysiology of menstrual bleeding

The circulating oestrogen levels in the body stimulate the proliferation of endometrium. Progesterone which is produced after ovulation from Corpus luteum transforms the proliferating endometrium into secretory. If pregnancy does not occur the secretory endometrium sheds in the form of menstrual bleeding a complex interaction between the hypothalamus pituitary ovarian axis and the outflow tract (uterus, cervix and vagina) is required for the normal menstrual bleeding to take place.

For a normal menstrual cycle to occur the following are required:

- Normal functioning hypothalamus GnRH secreted by hypothalamus.
- Normal functioning pituitary gland; hormone secreted from anterior pituitary FSH, LH.
- Normal functioning ovaries -synthesis of oestrogen and progesterone the entire spectrum of follicle development ovulation and formation of Corpus luteum occurs here.
- Normal endometrial development - endometrial lining which response cyclically to simulation by oestrogen and progesterone.
- An intact outflow tract essential for normal menstrual flow it requires a patent outflow tract and continuity of vaginal orifice vaginal canal and endocervix with uterine cavity.

Aim of the study- To determine the prevalence of etiologic causes of primary amenorrhea in western Rajasthan, Jodhpur

3. Materials and Methods

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This was a retrospective observational study.

Study Period -July 2019 to December 2019

Study Location- Dr. SNMC Jodhpur, Umaid Hospital, department of obstetrics and gynaecology

Methodology- Total 60 cases were included. A primary amenorrhea patient diagnosis can be made with the aid of history, physical examination, imaging studies, hormonal evaluation, karyotyping, history, age at onset of thelarche, cyclic abdominal pain, disorder of smell perception, family history, history of siblings age at Menarche, maternal age at menarche.

Personal examination -height, weight and blood pressure, breast development- tanner Staging, pubic and axillary hair-tanner Staging, external genitalia, clitoromegaly, signs of virilization, depth of vagina or bulging bluish membrane.

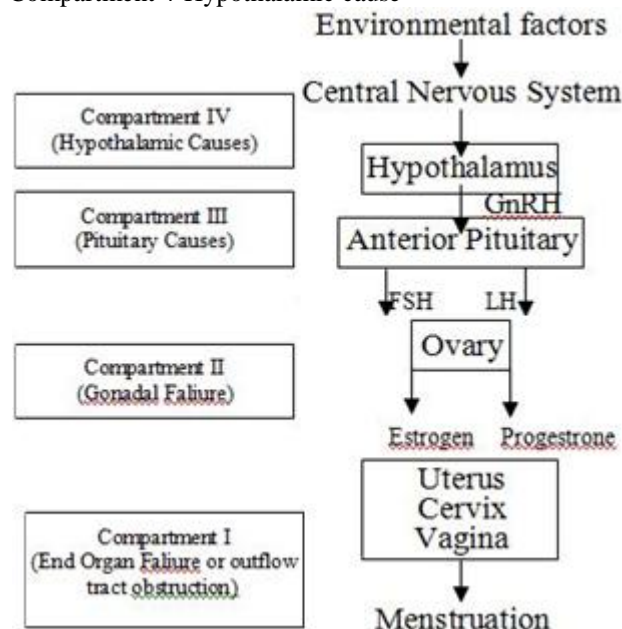
Imaging- Ultrasonography- presence or absence of uterus, HSG- uterine synechiae

CT or MRI- hypothalamic or pituitary cause

Hormonal evaluation- LH, FSH, serum prolactin, TSH

Karyotyping -MRKH 46XX, Turners- 45XO, AIS-46XY, gonadal dysgenesis -46XX, 46XY

The causes of primary ammenorrhoea are classified into 4 groups based on organs involved in the etiology.
 Compartment 1-End organ failure/outflow tract obstruction
 Compartment 2-Gonadal dysgenesis
 Compartment 3-Pituitary cause
 Compartment 4-Hypothalamic cause



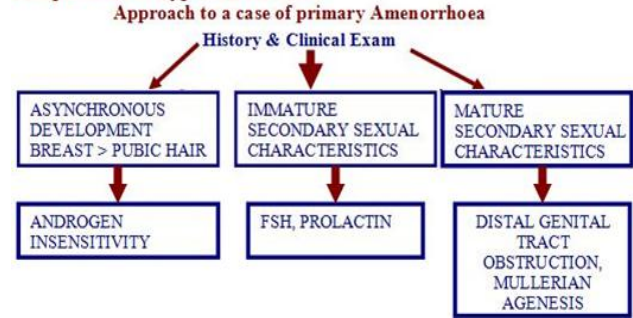
The causes of primary amenorrhoea are classified as:-

Compartment 1: End-organ failure or out-flow tract obstruction

Compartment 2: Gonadal failure

Compartment 3: Pituitary cause

Compartment 4: Hypothalamic cause



Results

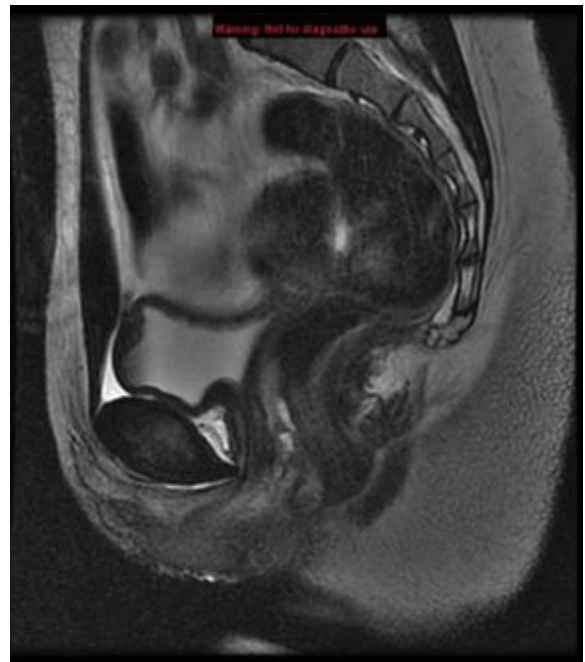
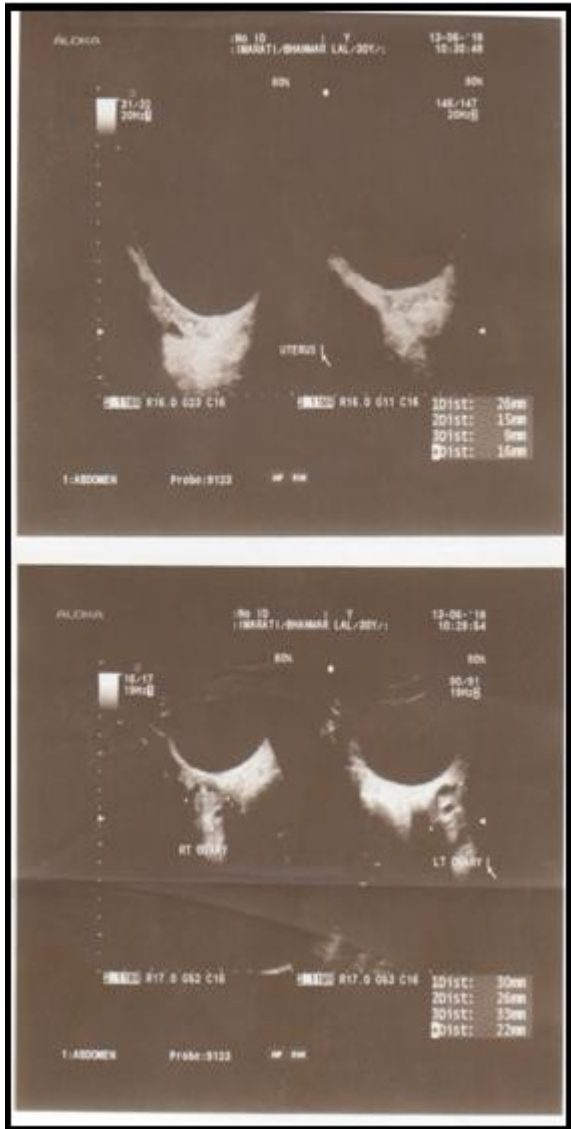
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- 4) Androgen insensitivity syndrome (AIS, 46XY) was found in three cases. (5%) In these cases bilateral gonadectomy done⁴.
- 5) There were two cases of Hyperprolactinemia⁵. (3.33%) Pt with low level of pituitary gonadotropins, decreased drive to ovaries for production for estrogens and progesterone, require exogenous gonadotropins for ovarian stimulation. And most of these patients conceive with ovulation induction.

There were two cases of hypogonadotropic hypogonadism and three cases PCOD (Polycystic ovary syndrome). These Pt were given ovulation induction with gonadotropins.

Table 1: Causes of primary amenorrhoea according to the comparative involved in the etiology

Serial Number	Causes	No. of cases	Percentage %
1	Compartment 1- (End organ failure)	50	83.33
a)	Mayer Rokitansky Kuster Hauser	30	60
b)	Imperforate hymen	17	28.33
c)	Androgen Insensitivity Syndrome	3	5
2	Compartment 2	3	5
a)	46XX gonadal dysgenesis	2	3.33

b)	45, XO (Turner)	1	1.66
3	Compartment 3	2	3.33
a)	Hyperprolactinemia	2	3.33
4	Compartment 4	5	8.33
a)	Hypogonadotropic Hypogonadism (Cons. delay)	2	3.33
b)	Polycystic ovarian Syndrome	3	5



4. Discussion

Amenorrhoea is a symptom that reflects some underlying disease anywhere in the hypothalamic-pituitary-ovarian-uterine axis. There are different causes of primary amenorrhoea. It includes anomalies of mullerian development, gonadal dysgenesis, constitutional delayed puberty. Adolescent girls with primary amenorrhoea are brought to the gynecologist by their parents the defects have been compartmentalised and may lie within the uterus, ovaries, pituitary or hypothalamus. Genetic and chromosomal anomalies also contribute to a major portion of primary amenorrhoea especially in cases of gonadal failure.

- Previous studies have been reported from all over world indicating gonadal dysfunction is commonest factor followed by pituitary/hypothalamic disorder and out flow tract anomalies.
- Cytogenetic studies and karyotype helps in establishing diagnosis and guiding about treatment specially for physiological counselling and also important for decision for gonadectomy.
- In Asian African countries out flow tract anomalies are commonest cause.
- A large study from Thailand of 295 cases shows mullerian anomaly is the commonest cause.
- In our study we found that mullerian anomalies as the commonest cause of primary amenorrhoea followed by gonadal dysgenesis and hypogonadotropic hypogonadism. The difference in etiology due to environmental and racial or genetic influence.
- A study from Andhra Pradesh shows abnormal karyotype of 25.5% women presenting with primary amenorrhoea.
- We have reported this study to highlight etiology causes of primary amenorrhoea at a tertiary care centre in Western Rajasthan Jodhpur.

5. Limitations of study

- Is a retrospective study based on collection of data from the available medical records of the patients.

- All the patients with primary amenorrhoea are not registered in special clinic.
- It is a single centre study at tertiary care centre hospital.

6. Recommendation

- a) A clinical examination and investigations eg. USG at Second Trimester to rule out any congenital abnormality.
 - Webbed neck
 - Increased nuchal fold thickness
- b) AT birth - Meticulos examination of external genitalia for early diagnosis and timely intervention to prevent long term. Health and social problem.
- c) Proper growth of children.
Early diagnosis and treatment
- d) t eg. in case of imperforated hymen, AIS.
- e) Combined approach of gynecologist, endocrinologist, pediatrician and psychiatrist.

7. Acknowledgment

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Conflict of Interest-None declared

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