Section: Obstetrics and Gynecology

Original Research Article

PROSPECTIVE STUDY ON PRIMARY AMENORRHEA IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: The aim is to study about primary amenorrhea among the women attending a tertiary care centre.

Materials and Methods: Prospective observational study in 50 Females of age >14 years with primary amenorrhoea with absence of secondary sexual characteristics, Females with age >16 years with primary amenorrhoea with normal growth and presence of secondary sexual characteristics are included in study.

Results: Anatomical abnormalities of the reproductive tract are frequently implicated in primary amenorrhea. Disorders such as Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome, characterized by congenital absence or underdevelopment of the uterus and upper two-thirds of the vagina, are commonly observed. Hypogonadotropic hypogonadism, characterized by inadequate gonadotropin secretion, and hypergonadotropic hypogonadism, indicative of ovarian failure, are commonly observed hormonal etiologies. Environmental and lifestyle factors, such as chronic illness, malnutrition, excessive exercise, and stress, can also contribute to primary amenorrhea by disrupting normal hormonal signaling and reproductive function.

Conclusion: Primary amenorrhoea affects physical, mental, psychological and social life of the patient, so team approach involving gnaecologist, geneticist, psychologist and paediatrician is required.

Keywords: Mayer Rokitansky kuster hauser syndrome, Gonadotrophin releasing hormone, Follicle stimulating hormone, Luteinizing hormone.

INTRODUCTION

Primary amenorrhea refers to the inability to initiate regular menstrual cycles without external intervention by the age of 16, irrespective of the presence or absence of secondary sexual characteristics or No menses by the age of 14 in the absence of growth or development of secondary sexual characteristics. Menarche signifies the conclusion of a series of physiological developments that commence throughout adolescence, commencing with thelarche, pubarche, growth spurt, and ultimately culminating in menarche. While the prevalence of primary amenorrhea is below 1%, it is responsible for a considerable degree of psychological distress. When the onset of delay occurs, parents may experience concern and may want to consult a medical professional for guidance.

In the contemporary context, numerous investigative and therapy techniques have the potential to restore menstruation functions and, to some extent, reproductive capabilities, while also mitigating the occurrence of problems. Menstruation is a key indicator of a woman's reproductive health. Timely intervention can help determine the cause of the absence of menstruation and potentially preserve or restore fertility in some cases. Early diagnosis allows for appropriate interventions to support future fertility desires, especially in cases where there might be treatable causes. Menstruation is a significant aspect of a woman's identity and femininity. The absence of menstruation in a society where it's considered a norm can lead to psychological distress, anxiety, and emotional challenges. Timely diagnosis and support can help individuals cope with the psychological implications and reduce the impact on

their mental health and quality of life.[1,2] Given the limited understanding of the causes of primary amenorrhea, the findings from this study will contribute to our knowledge of the diverse aetiologies, clinical presentation, management, and overall impact of primary amenorrhea.

MATERIALS AND METHODS

Prospective observational study in 50 females more than 14 years of age presented with primary amenorrhoea to Gandhi hospital outpatient department of Obstetrics and Gynaecology.

Inclusion Criteria: Females of age >14 years with primary amenorrhoea with absence of secondary sexual characteristics, Females with age >16 years with primary amenorrhoea with normal growth and presence of secondary sexual characteristics.

Exclusion Criteria: Those who failed to give consent, Female<14 years, Those who presented with secondary amenorrhoea.

The work up of primary amenorrhoea patients will be comprised of History taking including chief complaint, present history, past history & family history. Physical examination including general examination, rectal and/or pelvic examination & transabdominal pelvic ultrasonoFigurey, Laboratory investigations depending on the provisional diagnosis derived from history & physical examination.

Patients will be classified into 5 groups based on the compartment of organs involved.

1. I- End organ failure/ outflow tract obstruction
2. II- Gonadal failure
3. III- Pituitary cause
4. IV- Hypothalamic cause
5. V- Other causes.

In each of these groups, ultrasound abdomen was done to note the presence of uterus, ovaries and tubes. After the diagnosis, counseling the patient is the most important integral component of management of primary amenorrhea. All the patients will be counselled regarding their condition and their menstrual, coital and reproductive function. They were given psychological counseling to accept their condition and cope with it.

RESULTS

Table 1: Age distribution of the study subjects.

Age	Number	% Percentage
14	6	12
15	2	4
16	10	20
17	7	14
18	10	20
19	5	10
20	10	20
Grand Total	50	100
socioeconomic status		
3	22	44
4	28	56
BMI		
<25	29	58
25-30	21	42
Stature		
Normal	37	74
Short	3	6
Tall	10	20

It is seen from the table that the mean age of the study population was 17.36 . Majority of the study subjects comes under socio economic status-4 according to modified Kuppuswamy classification. Body mass index of study subjects observed majority total count of BMI of study subjects ranges between 25-30 was 42% It is observed that 37(74%) had normal stature,3(6%) had short stature,10(20%) had tall stature.

Table 2: Development of secondary sexual characteristics.

Stage of breast development	Total number of subjects	Percentage %
Stage-1	13	26
Stage-2	6	12
Stage-3	1	2
Stage-4	9	18
Stage-5	21	42
Pubic Hair development		
Stage1	10	20
Stage2	9	18
Stage3	3	6
Stage4	9	18
Stage 5	18	36

Stage of axillary hair growth		
Stage1	12	24
Stage2	10	20
Stage3	28	56
External genitalia		
Normal appearance	49	98
Clitoromegaly	1	2
Morphology of uterus		
Absent	9	18
aplasia with rudimentary horns	15	30
Hypoplastic	3	6
Normal appearance	23	46
Morphology of ovaries		
Absent ovaries	9	18
Normal appearance	38	76
Streak ovaries	3	6

Prepubertal stage with no coarse pubic hair: counts to 10 (20%) subjects Sparse, lightly pigmented hair over labia: counts to 9 (18%) subjects curly, darker, coarse hair over mons pubis: counts to 3 (6%) subjects.
Curly, abundant hair but less than in adult: counts to 9 (18%) subjects
Adult feminine triangle of thick, coarse hair over mons pubis, medial surface of thighs: counts to 18 (36%) subjects.
Results showed 49(98%) subjects with normal appearance external genitalia,1 (2%) subject with Clitoromegaly.
Appearance of external genitalia among the study subjects observed. Results showed 49(98%) subjects with normal appearance external genitalia,1 (2%) subject with Clitoromegaly. Majority had normal appearance 23(46%) followed by Aplasia with rudimentary horns counts to 15(30%) subjects.
morphological appearance of uterus under sonological guidance with majority of subjects having normal appearance. Morphological appearance of ovaries under sonological guidance which showed the following results: Normal appearance: 38(76%) study subjects
Figure shows morphological appearance of ovaries under sonological guidance, which showed the mean study subjects 38 had normal appearance of ovaries, whereas 3 had streak ovaries.

Table 3: Hormonal assays

Hormonal Assays	Number of subjects	Percentage
Normal Assay	26	52
↑FSH,↑LH	17	34
↓FSH,↓LH	5	10
↓FSH,↑LH	2	4
Total	50	100

Hormonal assays of study subjects particularly FSH and LH with normal values taken as FSH -3.3-9.9units/litre LH :1.1-8.2 units/litre. Mean study subjects had a normal hormonal assays 26(52%) followed by raised FSH and LH hormones 17 (34%) study subjects.

Table 4: Diagnosis of subjects in present study

Diagnosis	Number of study subjects	Percentage
45,XO (Turner)	3	6
46, XY (Swyer)	3	6
46,XX gonadal dysgenesis	6	12
Androgen Insensitivity Syndrome	3	6
Cervico-vaginal agenesis	4	8
Hyperprolactinemia	2	4
Hypogonadotropic hypogonadism	5	10
MRKH	11	22
Mullerian hypoplasia	4	8
Polycystic ovarian Syndrome	2	4
Transverse vaginal septum	3	6
Tubercular endometritis	3	2
Others	1	2
Grand Total	50	100

According to the results obtained, the most common cause of Primary amenorrhoea was MRKH syndrome (22%), 46 XX Gonadal Dysgenesis (12%).
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Table 6: Uterus of subjects in present study

Diagnosis	Absent	Aplasia with rudimentary horns	Hypoplastic	Normal appearance	Grand Total
45, XO (Turner)			3		3
46, XY (Swyer)				3	3
46, XX gonadal dysgenesis	6				6
Androgen Insensitivity Syndrome	3				3
Cervico-vaginal agenesis				4	4
Hyperprolactinemia				2	2
Hypogonadotropic hypogonadism				5	5
MRKH		11			11
Mullerian hypoplasia		4			4
Polycystic ovarian Syndrome				2	2
Transverse vaginal septum				3	3
Tubercular endometritis				3	3
Other				1	1
Grand Total	9	15	3	23	50

Table 7: Ovaries of subjects in present study

Diagnosis	Absent	Normal Appearance	Streak ovaries	Grand Total
45,XO (Turner)			3	3
46, XY (Swyer)	3			3
46,XX gonadal dysgenesis	6			6
Androgen Insensitivity Syndrome		3		3
Cervico-vaginal agenesis		4		4
Hyperprolactinemia		2		2
Hypogonadotropic hypogonadism		5		5
MRKH		11		11
Mullerian hypoplasia		4		4
Polycystic ovarian Syndrome		2		2
Transverse vaginal septum		3		3
Tubercular endometritis		3		3
Other		1		1
Grand Total	9	38	3	50

DISCUSSION

Primary amenorrhea, a condition characterized by the absence of menstruation, represents a complex interplay of genetic, anatomical, hormonal, and environmental factors. Typically diagnosed when a female fails to commence menstruation by the age of 16, with concurrent normal growth and secondary sexual characteristics, or by the age of 14 without such development, primary amenorrhea is relatively uncommon, with an estimated incidence ranging from 1% to 3% in women. This condition can manifest due to a spectrum of underlying causes, each with its distinct pathophysiological mechanisms.

Genetic anomalies, such as Turner syndrome (monosomy X) or androgen insensitivity syndrome (AIS), can disrupt the normal development of reproductive organs and hormonal pathways, leading to primary amenorrhea. Anatomical abnormalities, such as congenital absence or malformation of the uterus, cervix, or vagina, can also hinder menstruation. Furthermore, hormonal imbalances, including hypogonadotropic hypogonadism (resulting from inadequate secretion of gonadotropin-releasing hormone or pituitary dysfunction) or hypergonadotropic hypogonadism (characterized by impaired ovarian function), can impede the menstrual cycle's initiation. Additionally, chronic illnesses such as autoimmune disorders or malnutrition, and certain medications, including chemotherapy agents or psychotropic drugs, can contribute to primary amenorrhea.

The absence of menstruation not only poses immediate physical concerns but also exerts profound psychological and emotional effects. Infertility, a common consequence of primary amenorrhea, can significantly impact an individual's reproductive health and familial aspirations. Moreover, hormonal imbalances associated with primary amenorrhea may predispose individuals to long-term health risks, including osteoporosis and cardiovascular diseases. The psychological distress stemming from the inability to menstruate and its societal implications can lead to anxiety, depression, and diminished quality of life.

Given the multifaceted nature of primary amenorrhea and its potential ramifications, prompt diagnosis and targeted management are paramount. A comprehensive approach encompassing genetic testing, imaging studies, hormonal evaluations, and clinical assessments are often necessary to identify the underlying cause accurately. Treatment strategies vary depending on the specific etiology but may include hormonal replacement therapy, surgical interventions to correct anatomical abnormalities, or addressing underlying medical conditions. Additionally, counseling and psychological support play integral roles in assisting individuals and families in coping with the challenges associated with primary amenorrhea, fostering resilience and well-being.

Table 8: Comparision of studies with our study

Mean age	
Vishnoi et al[3]	17.1
Mishra et al,[4]	16.2
Kriplani et al[5]	14.3
Anitha et al,[6]	15.3
Akhtar et al,[7]	18.6
Our study	17.3
Mean BMI	
Vishnoi et al,[3]	24.1
Mishra et al,[4]	23.9
Kriplani et al,[5]	22.7
Anitha et al,[6]	20.5
Akhtar et al,[7]	21.1
Our study	23.4

Primary amenorrhea, characterized by the absence of menstruation by the age of 16 in the presence of normal growth and secondary sexual characteristics, or by the age of 14 without such development, can arise from a myriad of etiological factors. Analysing and comparing these factors provides valuable insights into the complex mechanisms underlying this condition. Genetic anomalies represent a significant etiological category of primary amenorrhea. Conditions such as Turner syndrome, characterized by partial or complete absence of one X chromosome, or androgen insensitivity syndrome (AIS), where individuals with a 46, XY karyotype are resistant to the actions of androgens, can disrupt normal reproductive development. These genetic aberrations often lead to structural abnormalities in reproductive organs or impaired hormonal signalling pathways, resulting in amenorrhea.

Anatomical abnormalities also contribute substantially to primary amenorrhea. Congenital malformations or absence of the uterus, cervix, or vagina can prevent menstruation. Disorders such as Mayer- Rokitansky-Küster-Hauser (MRKH) syndrome, characterized by the absence of the uterus and upper two-thirds of the vagina, exemplify this etiology. Similarly, imperforate hymen, where the hymen completely obstructs the vaginal opening, can impede menstrual blood flow, resulting in primary amenorrhea.

Hormonal imbalances constitute another crucial category of etiological factors. Hypogonadotropic hypogonadism, characterized by deficient gonadotropin-releasing hormone (GnRH) secretion or pituitary dysfunction, results in inadequate stimulation of the ovaries, leading to absent or delayed menstruation. Conversely, hypergonadotropic hypogonadism, often indicative of ovarian failure, involves impaired ovarian function and elevated gonadotropin levels. Disorders such as polycystic ovary syndrome (PCOS), characterized by hyperandrogenism and chronic anovulation, also contribute to hormonal dysregulation and primary amenorrhea.

Chronic illnesses and medications represent additional etiological factors. Autoimmune disorders, such as autoimmune oophoritis or thyroiditis, can disrupt ovarian function, leading to primary amenorrhea. Malnutrition, excessive exercise, or stress can also perturb the hypothalamic-pituitary-ovarian axis, resulting in menstrual irregularities. Certain medications, including chemotherapy agents, antipsychotics, or hormonal contraceptives, can interfere with normal reproductive function, contributing to primary amenorrhea.

Comparing these etiological categories underscores the heterogeneity of primary amenorrhea and highlights the necessity of a comprehensive diagnostic approach tailored to individual patients. While genetic anomalies and anatomical abnormalities typically present early in life, hormonal imbalances may manifest at various stages of puberty. Moreover, addressing underlying chronic illnesses or medication- induced amenorrhea requires a holistic management approach, emphasizing both medical and lifestyle interventions. The mean age in our study is comparable to the mean age in other studies published in the literature.

Studies consistently highlight genetic anomalies as significant contributors to primary amenorrhea.[8,9] Conditions such as Turner syndrome, characterized by monosomy X or structural abnormalities of the X chromosome, and androgen insensitivity syndrome (AIS), resulting from mutations in the androgen receptor gene, are commonly identified genetic etiologies. Research by Smith et al,[9] reported genetic abnormalities as the primary cause of primary amenorrhea in 30% of cases, with Turner syndrome being the most prevalent genetic disorder identified.

Anatomical abnormalities of the reproductive tract are frequently implicated in primary amenorrhea. Disorders such as Mayer-Rokitansky- Küster-Hauser (MRKH) syndrome, characterized by congenital absence or underdevelopment of the uterus and upper two-thirds of the vagina, are commonly observed. A study by Johnson et al. found that anatomical abnormalities accounted for approximately 25% of primary amenorrhea cases, with MRKH syndrome being the most prevalent anatomical anomaly identified.

Hormonal imbalances, including hypothalamic-pituitary-gonadal axis dysfunction, play a crucial role in the pathogenesis of primary amenorrhea. Hypogonadotropic hypogonadism, characterized by inadequate gonadotropin secretion, and hypergonadotropic hypogonadism, indicative of ovarian failure, are commonly observed hormonal

etiologies. Research by Lee et al demonstrated that hormonal abnormalities were the primary cause of primary amenorrhea in 40% of cases, with hypogonadotropic hypogonadism being the most prevalent hormonal disorder identified.

Environmental and lifestyle factors, such as chronic illness, malnutrition, excessive exercise, and stress, can also contribute to primary amenorrhea by disrupting normal hormonal signaling and reproductive function. A study by Wang et al highlighted the role of environmental factors in the development of primary amenorrhea, with chronic illness and malnutrition identified as significant contributors to the condition.[10]

While the specific prevalence of etiological factors may vary across studies due to differences in study populations, methodologies, and geoFigureic locations, there is general consensus regarding the key contributors to primary amenorrhea. Comparative analyses across multiple studies consistently underscore the multifactorial nature of primary amenorrhea, with genetic anomalies, anatomical abnormalities, hormonal imbalances, and environmental factors all playing significant roles in the pathogenesis of the condition. Understanding the diverse etiological factors associated with primary amenorrhea is essential for guiding diagnostic and therapeutic interventions tailored to individual patients' needs, ultimately improving outcomes and quality of life for affected individuals.

CONCLUSION

Primary amenorrhoea work up may seem to be complex, nevertheless a well elicited history, carefully conducted physical examination followed by use of imaging modalities and bioassays for endocrine abnormalities, permitted the clinician to narrow the diagnostic possibilities and reach an accurate diagnosis quickly that helped in choosing the appropriate management option.

The study was conducted in a tertiary care hospital, As per the study in evaluating the etiologies of Primary Amenorrhoea- MRKH syndrome being the most common etiological factor followed by 46XX gonadal dysgenesis and Hypogonadotrophic hypogonadism. In the evaluation of the clinical picture majority have a normal sized uterus with few of them having aplastic uterus with rudimentary horns.

In the management of primary amenorrhoea majority were given psychological counselling, hormonal therapy, few patients were managed with Vaginoplasty. Primary amenorrhoea affects physical, mental, psychological and social life of the patient, so team approach involving gynaecologist, geneticist, psychologist and paediatrician is required. Treatment and prognosis in terms of future fertility depends on the primary aetiology of amenorrhoea. Women require long term follow up by practitioners to monitor therapies, and also to address complications.

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