

## Klinefelter Syndrome “A Chromosomal X Karyotype disorder”

Ankit Verma\*, Aryan kumar, Vintesh kumar Sharma  
IIMT College of Pharmacy, Greater Noida-201310

Submitted: 05-05-2022

Accepted: 15-05-2022

### ABSTRACT

Klinefelter syndrome is a group disorder in which there is an extra X chromosome occur in male karyotype. Differentiation between normal child and KS child is very difficult in age below 7yr. 47,XXY aneuploidy is the most commonly seen in this disorder with a prevalence rate of one in 500 male child. Other sex chromosomal aneuploidy like 48,XXYY and 48,XXXYY have also been described but they are much less frequent. Occurrence of this syndrome is due to error in the chromosome non-disjunction during parenteral gametogenesis as a result a sperm or an egg carries extra X chromosome in addition to the normal single sex chromosome. School age child is associated with language delay, learning disabilities or behavioral problems, adults are often associated with low level of androgen, small testes, gynecomastia and many other symptom. Androgen replacement therapy is used to control or reduce the symptom, the most crucial time to initiate this therapy is before puberty at the age of 10-11 years.

**Keywords:** Androgen, Azoospermia, chromosome, gynecomastia, hypogonadism, meiosis

### I. INTRODUCTION

Klinefelter's syndrome is a genetic disorder/or chromosomal disorder in which a male individual born with an extra X chromosome which is abnormal when compared it to normal individual born with 23 pair of chromosome where XY chromosome is present but in klinefeltersyndromic person it is associated with (47, XXY) chromosome. This condition is also called as XXY syndrome. This type of abnormality is not detected during childhood because it is not possible to distinguish the normal child with hypogonadism child. Diagnosis of this type of condition is possible only during puberty or adolescence or the age of maturity. It is found that men with this type of syndrome is infertile by birth. It is found that klinefelter syndrome affect over 500 male people, it results in testicular failure, androgen deficiency, impaired spermatogenesis<sup>(1)</sup>. In chromosomal study of suspected individual, it is found that other extra

chromosome is also present like 48,XXYY; 48,XXXYY; and 49,XXXXYY.

### History of Klinefelter syndrome

This syndrome was named after American endocrinologist Harry Klinefelter. Klinefelter syndrome was first described when Jacobes et al. recognized that syndrome occurs due to the chromosomal disorder in which an extra X chromosome is present. Until 1959, it is thought that it can occur due to endocrine disorder of unknown etiology. In 1942 Dr Klinefelter recognized 9 male individuals with symptoms like gynecomastia, small testis, azoospermia and increased gonadotropin levels. They believed that failure in the Sertoli cell of the testis causes hypogonadism. They also suggest that these patients had low or absent level of a putative second testicular hormone, which regulates the level of pituitary gonadotropins by feedback inhibition and which they labeled X hormone or inhibin<sup>(2)</sup>.

### Synonyms

Ks, 47,XXY, XXY Syndrome, XXY Trisomy, 3+X Chromosome with Y, Trisomic disorder.

### Epidemiology

Klinefelter syndrome is the most common chromosomal disorder seen only in males with an estimated frequency of 1:500- 1:1000 male child birth<sup>(3)</sup>. It is characterized by X chromosome polysomy with X disomy, trisomy. 47,XXY is the most common variant<sup>(4)</sup>. Almost all men with a 47,XXY karyotype will be infertile; Klinefelter syndrome possesses 3 percent of male infertility<sup>(5)</sup>.

### Sign & Symptom

Oligospermia and azoospermia are most commonly in Klinefelter syndrome infertile patients<sup>(6)</sup>. Affected men also have small testes, decreased facial hair, gynecomastia, decreased pubic hair, small penis, Tall, slender body habitus with long bones and shorter torso, motor delay and dysfunction, speech and language difficulty, attention difficulties, learning disabilities, Dyslexia, Psychosocial or behavioral problems.

Androgen deficiency cause loss of libido, decreased muscle bulk and tone, decreased bone mineral density etc<sup>(7)</sup>.

#### Etiology

The extra chromosome found in Klinefelter syndrome is mainly occur due to an error of non-disjunction during parenteral gametogenesis as a results a sperm or an egg carries extra X chromosome in addition to the normal single sex chromosome<sup>(8)</sup>. It also may results due to error in the division during mitosis in the zygote<sup>(9)</sup>. A study using DNA probes found that paternal non-disjunction posses 53% of case, maternal meiotic I error posses 34.5% of case, maternal meiotic II error posses 9.5% of case and postzygotic mitotic error posses only 3% case<sup>(10)</sup>. There is a positive coorelation between maternal age and maternal meiotic I error. The error in the gametogenesis of both maternal and paternal is equally responsible for the causing the 47,XXY disorder<sup>(11)</sup>.

#### Diagnosis

Testicular biopsy specimen of infants with this disorder describe only a reduced number of germ cell. After the puberty pathologic changes like hyalinization, fibrosis of the seminiferous tubules small shrunken testes and azoospermia are major characteristics<sup>(12)</sup>. There is also decreased in level of inhibin B observed due to loss of functional seminiferous tubule and sertoli cell. It is the hormone which regulate the level of FSH<sup>(13)</sup>. The presence of increased serum LH level despite low-normal testosterone level indicate that patients with KS have an altered hypothalamic pitutary-gonadal axis<sup>(14)</sup>.

#### Treatment

There are no cure for KS but most of the problem arised like decreased libido, weakness, decreased bone density, and androgen deficiency can be reduced by the use of testosterone replacement therapy.

Testosterone replacement therapy is used in this syndrome, despite of it has no effect on infertility but it correct the androgen deficiency<sup>(15)</sup>. This therapy results in increase in facial and pubic hair, a more masculine distribution of body fat, increased libido, and bone mineral density<sup>(16)</sup>. At the time of begining of puberty is the optimal time for the initiation of testosterone replacement therapy because this timing boys with KS experience a pubertak changes similar to their peers and allows testosterone to have it most marked effect on bone mineral density<sup>(17)</sup>. This treatment therap has no effect on testicular size or spermatogenesis, and it usually does not reduce

gynecomastia, which can be very well treated with plastic surgery.<sup>(18)</sup>

## II. CONCLUSION

Klinefelter syndrome is a an extra X chromosomal syndrome in which a male child posses an extra X chromosome which may leads to differentiation among normal child after the puberty. Better understanding of inactivation of X chromosome, regulation of meiosis as well as pathophysiology related to spermatogonia allow the researcher to develop better therapeutic management approach for this syndrome.

## REFERENCES

- [1]. Leonard JM, Bremner WJ, Capell PT, Paulsen CA. Male hypogonadism: Klinefelter and Reifenstein syndrome. *Birth Defect*. 1975;11:17-22.
- [2]. Klinefelter HF Jr, Reifenstein EC Jr, Albright F. Syndrome characterized by gynecomastia, aspermatogenesis without a-Leydigism and increased secretion of follicle-stimulating hormone. *J Clin Endocrinol Metab*. 1942;2:615-622.
- [3]. Lanfranco F, Kamischke A, Zitzmann M, Nieschlag E. Klinefelter's syndrome. *Lancet* 2004;364:273-283.
- [4]. Graham JM Jr, Bashir AS, Stark RE, et al. Oral and written language abilities of XXY boys: implication for anticipatory guidance. *Pediatrics* 1988;81:795-806.
- [5]. Zollner TM, Veraart JC, Wolter M, Hesse S, Villemur B, Wenke A, et al. Leg ulcers in Klinefelter's syndrome-further evidence for an involvement of plasminogen activator inhibitor-1. *Br J Dermatol* 1997;136:341-4.
- [6]. Simpson JL, Graham JM jr, Samango-sprouse C, Swerdloff R. Klinefelter syndrome. In: Cassidy SB, Allanson JE. *Management of genetic syndrome*. 2d ed. Hoboken, N.J, Wiley & sons, 2005:323-33.
- [7]. Lanfranco F, Kamischke A, Zitzmann M, Nieschlag E. Klinefelter's syndrome. *Lancet* 2004;364:273-83.
- [8]. King RA, Potter JI, Motulsky AH. *The genetic Basis of common disease*. New York, NY: Oxford University Press; 1992:876-894.
- [9]. Paulsen CA, Gordon DL, Carpenter RW, Gandy HM, Drucker WD. Klinefelter's syndrome and it's variants: a hormonal and chromosomal study. *Recent Prog Horm Res*. 1968;24:321-363.



- [10]. Jacobs PA, Hassold TJ, Whittington E, et al. Klinefelter's syndrome: an analysis of the origin of the additional sex chromosome using molecular probes. *Ann Hum Genet.* 1988;52:93-109.
- [11]. Klinger HP, Ludwig KS. A universal stain for the sex chromatin body. *Stain Tech.* 1957;3:235-244.
- [12]. Winter JSD. Androgen therapy in klinefelter syndrome during adolescence. *Birth Defect.* 1991;26:234-235.
- [13]. Anawalt BD, Bebb RA, Matsumoto AM, et al. serum inhibin B level reflect sertoli cell function in normal men and men with testicular dysfunction. *J Clin Endocrinol Metab.* 1996;81:3341-3345.
- [14]. Lipsett MB, Wilson H, Kirschner MA, et al. Studies on Leydig cell physiology and pathology: secretion and metabolism of testosterone. *Recent Prog Horm Res.* 1966;22:245-270.
- [15]. Matsumoto AM. Hormonal therapy of male hypogonadism. *EndocrinolMetab Clin North Am.* 1994;23:857-875.
- [16]. Becker KL. Clinical ana therapeutic experience with klinefelter's syndrome. *Fertil Steril.* 1972;23:568-578.
- [17]. Schibler D, Brook CGD, Kind HP, Zachmann M, Prader A. Growth and body proportion in 54 boys and men with klinefelter's syndrome. *Helv Paediatr Acta.* 1974;29:325-333.
- [18]. Myhre SA, Rluvalcaba RHA, Johnson HR, Thuline HC, Kelley VC. The effect of testosterone in klinefelter's syndrome. *J Pediatr.* 1970;76:267-276.