



Research Article

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# Klinefelter Syndrome is Not an Inherited Condition



**Siniša Franjić\***

Independent Researcher, Europe

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**\*Corresponding author:** Siniša Franjić, Independent Researcher, Europe, Email: sinisa.franjic@gmail.com

## Abstract

Klinefelter syndrome has  $\geq 2$  X chromosomes in addition to 1 Y chromosome, leading to the development of a male phenotype. Klinefelter's syndrome appears in about 1/800 live births of male children. Affected boys are usually tall, with disproportionately long arms and legs. They often have small, firm testicles, and about 30% of them develop gynecomastia. Puberty usually occurs at the usual age, but facial hair is often poorly expressed. There is a tendency for learning difficulties and many show lower verbal IQ, weaker processing of auditory information and difficulty reading. The difference in clinical pictures is great, and many men with 47, XXY have normal appearance and intellect. Many cases are discovered during infertility treatment. Testicular development extends from hyalinized non-functional tubules to definite spermatogenesis; urinary excretion of follicle-stimulating hormone is often increased. In 15% of cases, it is mosaicism, and these men can be fertile. Some affected men have 3, 4 or even 5 X chromosomes in addition to the Y chromosome. With an increase in the number of X chromosomes, the expression of mental retardation and malformations increases.

**Conclusion:** Gynecology and Obstetrics related cases have markedly been managed at Benazir Bhutto Hospital.

**Keywords:** Klinefelter Syndrome; IQ; ID; Signs; Pathogenesis; Health

**Abbreviations:** KS: Klinefelter Syndrome; CHH: Congenital Hypogonadotropic Hypogonadism; QoL: Quality of Life; CT: Computed Tomography; EEG: Electroencephalogram; TESE: Testicular Sperm Extraction; ICSI: Intracytoplasmic Sperm Injection; LH: Luteinizing Hormone; FSH: Follicle Stimulating Hormone

## Introduction

Klinefelter syndrome (KS) is the foremost common chromosomal anomaly in guys (1: 660) coming about in an atypical number of X chromosomes-most commonly 47XXY [1]. Hallmark signs incorporate little testicles, gynecomastia (breast tissue improvement), learning troubles, and infertility. While CHH (Congenital Hypogonadotropic Hypogonadism) is biochemically characterized by hypogonadotropic hypogonadism (i.e., central/neuroendocrine deformity), KS is checked by hypergonadotropic hypogonadism (i.e., essential gonadal failure). Introduction changes broadly extending from generally gentle (mosaicism) to more complex circumstances showing more extreme signs and side effects. Strikingly, it is assessed that up to 75% of influenced men are not analyzed. Less than 10% are distinguished earlier to adolescence. Ordinarily, KS becomes apparent at adolescence when hypogonadism is recognized within the setting of fizzled or slowed down pubertal movement. Boys with KS may have issues

with muscle coordination and development, moo muscle tone, destitute fine engine abilities, postponed discourse, learning difficulties, and official brokenness (i.e., destitute self-control, self-regulation) that will disable scholastic achievement. Shifting degrees of cognitive, social, behavioral, and learning troubles may be shown and boys with KS can advantage from extraordinary instruction programs and neuropsychological treatment. Thinks about show that men with KS frequently have noteworthy mental horribleness and as often as possible battle with psychosocial results of KS coming about in impaired QoL (Quality of Life).

## Description

The classical depiction incorporates mental hindrance, hypogonadism and gynecomastia [2]. They are on a normal 10 cm taller than XY males. The modified body extent is with low upper to lower fragment proportion. Cells going astray from the products of the haploid number are called aneuploid, demonstrating a lost

or additional chromosome. This happens most regularly from the meiotic nondisjunction of an X-chromosome. In 54% it may be maternal in beginning, and in 46% it is fatherly in root. These people have a male karyotype with additional X-chromosome, i.e., 47, XXY. The phenotype is male. When the number of X-chromosome surpasses two, mental hindrance and disability of virilization is more. Happening in 1 in 580 infant males, KS is the foremost common genetic cause of hypogonadism and fruitlessness in men [3]. It is caused by the nearness of an additional X chromosome (47, XXY). The additional chromosome emerges from nondisjunction in either the sperm or egg. About 15% of guys with highlights of KS are found to be mosaic, with 46, XY/47, XXY mosaicism being the foremost common. Sometime recently adolescence, males with KS are phenotypically indistinguishable from the rest of the populace.

The conclusion is frequently made in puberty when the hallmark of the condition, beneath and rogenation within the nearness of testicles that stay puerile in volume, ought to alarm the clinician. Youthful grown-ups with KS tend to be tall with long appendages. During puberty or adulthood, gynecomastia may happen. Since of failure of growth and maturation of the testicles, males with KS have hypergonadotropic hypogonadism and failure to deliver reasonable sperm. Low production of testicular testosterone comes about in failure to totally create auxiliary sexual characteristics, such as facial hair, developing of the voice, and charisma. In adulthood, osteopenia and osteoporosis create. Since these discoveries, testosterone supplementation is demonstrated. Most males with KS are fruitless since they deliver few practical sperm. Through the utilize of microdissection testicular sperm extraction, a strategy in which reasonable sperm are confined from testicular tissue, coupled with in vitro fertilization and intracytoplasmic sperm infusion, it is conceivable for men with KS to father children; all children born to these men utilizing this innovation have had a ordinary chromosome complement.

### IQ and ID

Klinefelter syndrome (KS) is caused by the nearness of an additional X chromosome in a male [4]. Males with KS have the combination of testicular failure, tall stature for the family, and a moderately characteristic cognitive and behavioral profile. Cognitively, boys with KS tend to be within the ordinary extend, but IQ scores tend to be less than those of their kin or control males. The writing reports that most guys with KS have lower verbal IQ than execution IQ, although the degree of distinction can change over the life expectancy; in expansion, a few ponders have found the switch in that execution IQ is lower than verbal IQ. In expansion, a later consider found that the lower full-scale IQ is inferable to shortfalls in both verbal and nonverbal cognitive abilities. It isn't astounding hence that dialect and discourse impairments are moreover common and are show at all ages. Discourse and dialect delays, as proven by delays in early expressive dialect and discourse milestones, are noted in most guys

with KS. Within the early school a long time, issues with perusing, spelling, and composing (but not arithmetic skills) are common. In expansion, these boys have troubles with verbalization, word finding, and phonemic preparing. During the moment decade, disabled perusing, spelling, and number-crunching are predominant, with most of these boys accepting extraordinary instruction. In early adulthood, these gaps widen, with KS males being a few review levels below age-matched controls. In expansion, boys with KS moreover have the next recurrence of engine issues, as illustrated by diminished quality, running speed, and agility. The determination of ID depends upon assessment of the child's psychosocial abilities and a audit of school reports, and may require formal IQ testing [5]. A assurance of whether formal testing ought to be performed is based on physical examination discoveries, formative and school histories, and concerns of the family and instructors. Males with Klinefelter disorder regularly have formative delay, particularly in verbal cognitive ranges where they underachieve in perusing, spelling, and arithmetic; their full IQ may be typical, but their verbal IQ is ordinarily diminished. Boys with Klinefelter syndrome frequently go unidentified until adolescence because of the subtleness of the clinical discoveries. The conclusion ought to be considered for all boys (regardless of age) who have been recognized as having mental incapacity, or psychosocial, school, or adjustment issues.

Physical findings to be considered in patients with suspected ID incorporate the measure of the occiput, abnormal hair color or dispersion, eye shape and situation, contorted ears or nose, and variations from the norm in jaw measure, mouth shape, or sense of taste tallness. The hands and feet may have brief metacarpals or metatarsals, covering or supernumerary digits, irregular palmar wrinkles, or nail changes. The skin may have café au lait spots or depigmented nevi, and the genitalia may be strangely measured or ambiguous. Patients with Klinefelter syndrome are regularly tall and lean with long limits. The testicles and phallus are frequently little for age, but this may not get to be clear until adolescence. As grown-ups, males with Klinefelter syndrome create gynecomastia, inadequate facial hair, and azoospermia. The rate of breast cancer and a few hematologic cancers is hoisted in Klinefelter syndrome. Research facility testing of a child with ID is based on clinical discoveries and formative points of reference. A chromosomal examination is regularly included within the assessment of a child with ID on the off chance that a hereditary or syndromic cause is suspected; for Klinefelter disorder such an investigation will most frequently illustrate one additional X chromosome (47, XXY) but may appear extra X chromosomes (48, XXXY) or mosaicism (46, XY/47, XXY). Other ID testing may incorporate pee and serum amino and natural acids, serum levels of smelling salts, lead, zinc, and copper, and serum titers for intrinsic contaminations. Radiologic assessment may incorporate cranial computed tomography (CT), attractive reverberation imaging (MRI), or electroencephalogram (EEG).

## Signs

People with Klinefelter syndrome tend to have longer arms and legs, with a low upper-to-lower fragment ratio [6]. Biacromial distance across is additionally low, likely auxiliary to low testosterone levels. Tallness ranges from the 25<sup>th</sup> to the 99<sup>th</sup> percentile for age, whereas cruel stature is at the 75<sup>th</sup> percentile. Most of the pickup in stature takes put between the ages of 5 and 8 a long time. Head circumference and weight are often at the 50<sup>th</sup> percentile. During childhood, testicular volume and penile length are somewhat lower than ordinary. Afterward in advancement amid puberty, testicular estimate remains little, with a length as a rule less than 2.5 cm and normal volume of less than 4 mL. Numerous people will enter adolescence ordinarily, but testosterone levels tend to diminish in late puberty to adulthood. Inadequate sum of androgens shows, ordinarily less than half the level seen in unaffected people, auxiliary sexual characteristics don't totally create and virilization is lacking. Inadequate body and facial hair are shown, in conjunction with gynecomastia, in more than half of youthful patients. Most patients are barren, with hyalinization and fibrosis of the seminiferous tubules by mid-puberty. Although as it were a minority of people with Klinefelter disorder have practical sperm within the ejaculate, and in this way can supply sperm for cryopreservation, later propels in regenerative innovation counting testicular sperm extraction (TESE) and intracytoplasmic sperm injection (ICSI) have essentially expanded their regenerative potential. Fifth finger clinodactyly is the foremost common minor inconsistency and is display in nearly one-third of patients. Cleft sense of taste, cryptorchidism, and inguinal hernia are other major inconsistencies. Other variations from the norm detailed are mitral valve prolapse, scoliosis, expanded recurrence of incessant bronchitis and diabetes mellitus, extreme skin break out, and hypospadias.

## Patient

These patients approach the specialist, with the failure of improvement of auxiliary sexual characters [2]. These patients tend to be tall and underweight. They generally have stretched legs. The testicles tend to be little for the age, and the phallus tend to be littler than normal. Cryptorchidism and hypospadias may moreover happen. Improvement of adolescence is deferred. Feminine dispersion of the pubic hair is displayed. Forty percent of the grown-ups will have gynecomastia showing up ordinarily before long after adolescence between ages of 14 and 16 a long time. The foremost common testicular injuries are spermatogenic capture and Sertoli cell prevalence. The testicles are little with the cruel length of 1.8 cm as compared to 5.1 cm in typical male. The testicles appear ordinarily development early in adolescence, but it stops in midpuberty. Testicles are contracted and hyalinized seminiferous tubules. A few are lined by Sertoli cells. Hypertrophy and clamping of Leydig cells are shown. Azoospermia and fruitlessness are experienced. Antisperm antibodies have been identified. The diagnosis is commonly made in adolescence.

Typically, since of subtleness of clinical sign in childhood. Other highlights such as behavioral or psychiatric unsettling influences, learning and school alteration issues ought to be assessed to run the show out this disorder. These children may be on edge, forceful, and engage in reserved acts. There will be verbal cognitive defects and underachievement in perusing, spelling and arithmetic. There's an expanded rate of aspiratory infection, varicose veins, cancer breast, diabetes mellitus and peptic ulcers. Lymphomas and leukemias are related. Extragonadal germ cell tumor particularly of the mediastinum, cerebral hemangiomas happen with tall recurrence.

## Pathogenesis

The aberrations within the number of sex chromosomes happening in Klinefelter syndrome are caused by nondisjunction, most commonly during fatherly meiosis I [6]. This instrument accounts for roughly 50% of the cases, with the rest of them ascribed to blunders in maternal meiosis I, or maternal meiosis II. Fatherly blunders can happen during meiosis I, since this can be as if it were instrument that can create a gamete with both the X and the Y chromosome show. A mistake happening in fatherly meiosis II, when X and Y are as of now isolated, can as it were delivering gametes with XX or YY chromosomes that, in combination with a typical oocyte, would result in a XXX or XYY karyotype. The proof behind blunders in fatherly meiosis isn't as clear, with a few ponders recommending that more seasoned fathers have the next propensity to create XY sperm, whereas others have appeared no influence of age on XY recombination. Since the female oocyte carries as it were X chromosomes, blunders happening either in meiosis I or II can deliver gametes with 2 X chromosomes and thus a zygote with XXY karyotype. Most maternal mistakes happen in meiosis I. An association of aneuploidy with progressed maternal age has been detailed, although it has been seen with blunders happening amid meiosis I; meiosis II blunders don't appear to be more common with expanding maternal age. A postzygotic mitotic mistake can moreover contribute to the Klinefelter phenotype in a little number of cases. A few patients have been found to have a mosaic karyotype, counting cells with XY and XXY. The degree of mosaicism changes between patients and indeed between diverse tissue tests of the same quiet. People with XXY/XY mosaicism tend to have a much better prognosis for testicular function.

Klinefelter syndrome has phenotypic inconstancy since of the X chromosome inactivation that regularly takes put in all human cells that contain more than 1 X chromosome. All but 1 X chromosome undergo inactivation per Lyon theory (with the arrangement of a break even with number of Barr bodies) and typically the component by which overexpression of qualities found on the X chromosome is avoided. Within the case of Klinefelter disorder, as in a few other genetic conditions, the method of inactivation does not happen haphazardly, but a particular X chromosome, either fatherly or maternal, tends to be inactivated more regularly. This can be a handle known as particular or skewed X chromosome

inactivation and has imperative clinical suggestions. The androgen receptor quality AR, by which testosterone applies its activity, is found on the X chromosome and contains a trinucleotide (CAG) repeat grouping. Each X chromosome contains a distinctive number of CAG repeats within the AR quality, and shorter numbers of repeats have been related with way better reaction to androgen treatment and higher level of instruction compared to longer repeats. Most patients with Klinefelter disorder have been appeared to have the X chromosome with the shorter CAG repeat number specially inactivated; in this way, the allele with the longer CAG repeats is dynamic in most cells and is thought to be the cause of hypogonadism in most patients with Klinefelter syndrome. Klinefelter syndrome comes about in a frame of essential testicular disappointment, diminished testosterone generation, and hence raised levels of gonadotrophin luteinizing hormone (LH) and follicle stimulating hormone (FSH). Testicular function can be extraordinarily diminished from fetal life, although in most patients it remains at ordinary levels until adolescence when a noteworthy increment in gonadotrophin levels is famous with a concomitant diminish of testosterone generation within the lower levels of typical.

## Diagnosis

It ought to be suspected in prepubertal children, who have long legs, smaller than typical testicles, little phallus, learning disarranges, delay in dialect improvement, mental retardation, or psychosocial behavioral issues [2]. Gonadotropins are lifted, testosterone levels are somewhat low. Estradiol levels are raised and account for gynecomastia. Chromosome examination uncovers 47, XXY karyotype. Testicular biopsy appears lack and nonattendance of germinal cells some time recently adolescence. After adolescence seminiferous tubules are hyalinized and contracted. There's adenomatous clumping of Leydig cells. There's prevalence of Sertoli cells. The testosterone concentration is low. The concentration of estradiol is ordinary or expanded and gonadotropin concentration is raised. Gynecomastia occurs in 40-50% of cases because of expanded proportion of serum estradiol to testosterone. Breast cancer happens in 4% of patients and the rate is 20 times higher than in typical guys.

## Management

Substitution treatment with long-acting testosterone arrangements is suggested [2]. It ought to start at 11-12 a long time of age. The enanthate ester may be utilized. The beginning measurements is 25-50 mg given intramuscularly each 3-4 weeks. The increase of 50 mg is done once in each 6-9 months till the support measurements of grown-up is gotten. The support dosage of grown-up is 250-300 mg each 3 weeks. Children XXY/XY mosaicism have way better guess. As the number X chromosomes increments past two, the clinical sign increases correspondingly. Management incorporates behavioral and psychological rehabilitation.

## Transitional Care

Standard treatment is deep rooted testosterone substitution, however evidence-based treatment suggestions are lacking [1]. Information recommend that early start of testosterone substitution combined with extraordinary instruction and family back can make strides behavioral working in youthful men with KS. Long-term results of KS on wellbeing incorporate destitute bone health (osteopenia/porosis), metabolic issues (weight, metabolic disorder, type 2 diabetes), vascular infection (i.e., hypostatic ulceration, deep-vein thrombosis, aspiratory embolism), expanded chance for breast cancer, and immune system illness. Unconstrained richness is exceedingly uncommon and close incomprehensible. Later propels in helped propagation (i.e., testicular microdissection with intracytoplasmic sperm infusion [microTESE-ICSI]) can make ripeness a plausibility in generally half of cases. Hence, for youthful grown-ups with KS, key components of transitional care incorporate illness administration tending to barrenness and psychosocial well-being. A few surveys have advertised direction on transitional care in this quiet populace. The common agreement incorporates an accentuation on multidisciplinary administration to address therapeutic issues, instructive and professional needs, and mental wellbeing angles of KS. Strikingly, clinician analysts from Denmark have as of late distributed formatively fitting care suggestions for KS. Interests, the University Hospital in Copenhagen (Rigshospitalet) features a "cradle to grave" clinic for patients with KS where move is between suppliers inside the same institution.

There is a meager information on the adequacy of transitional care in KS. A special case is the Children's Hospital of Colorado intrigue clinic for children and teenagers with sex chromosome aneuploidy "eXtraordinary Kids Clinic". This organized program gives comprehensive multi-specialty care that incorporates developmental-behavioral pediatrics, endocrinology, genetic counseling, child brain research, pediatric neuropsychology, speech-language pathology, word related treatment, nursing, and social work. The program moreover gives instruction, family back, and promotion. A persistent study demonstrated wide appreciation of the interprofessional approach and profoundly esteemed the learned clinical facilitator. In addition to that, 85% of families were "very satisfied" and 9.8% were "satisfied" recommending adequacy and adequacy. Such a multidisciplinary approach is vital as guardians frequently feel formally dressed, have trouble exploring different specialties and need back in making choices approximately their child's care. In fact, the complex blend of physical, cognitive, behavioral, and mental angle of KS presents one-of-a-kind challenges for successful transitional care.

## Conclusion

Klinefelter syndrome is not an inherited condition. Instead, the extra sex chromosome is the result of random errors during egg or sperm formation or after conception. Many men with Klinefelter

syndrome have few visible symptoms, and the condition may go undiagnosed until adulthood or puberty. In others, the syndrome is noticeable in terms of growth and appearance. In addition, it can cause problems in speech and learning, which is visible even at an earlier age..

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