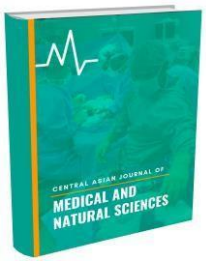

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Article

Unlocking Male Infertility Genetic and Hormonal Insights for Treatment Advancements

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Abstract: Infertility affects many men and women, with male infertility often resulting from azoospermia (complete absence of sperm) and oligospermia (low sperm count and motility). Genetic and endocrine factors are primary causes of infertility. This study aimed to investigate genetic causes and hormone levels in male infertility. We analyzed 423 infertile male patients at Al-Kut Hospital's IVF Center, focusing on hereditary sex hormone levels and abnormal karyotypes. Abnormal karyotype incidences in azoospermia and oligospermia were 7% and 23%, respectively. Among azoospermic patients, 62.7% exhibited (47,XXY) Klinefelter syndrome. Elevated FSH and LH levels were noted in azoospermic patients with abnormal karyotypes compared to testosterone levels in other groups. The study highlights the strong link between azoospermia and genetic chromosomal abnormalities, suggesting that hormone levels (testosterone, LH, FSH) in azoospermic patients with abnormal karyotypes are valuable for genetic studies, medical consultations, and assisted reproductive technologies.

Keywords: Karyotype, Sex Hormones, (FSH) Follicle-Stimulating Hormone, testosterone, (LH) Luteinizing Hormone, Genetic Counseling, Infertility, Azoospermia, Oligoasthenospermia

1. Introduction

Infertility is defined as the inability to achieve pregnancy after twelve months of regular intercourse. The male-related factor represents about (50 to 60)% of all infertility cases, but it represents only (10 to 20)% of couples [1]. The prevalence of Chromosomal and structural abnormalities in patients suffering from infertility range from (2.5)% to (11)%. 2.5 Thus, it is considered a common genetic defect that may be responsible for about 1.6%. of male infertility cases is Klinefelter syndrome [2].

Male patients suffering from infertility Abnormal hormone levels can be used to help diagnose sperm formation disorders in patients. Many researches have proven that hormones can be relied upon to treat delayed childbearing in male patients.

2. Materials and Methods

Clinical Data. Infertile male patients who were examined and diagnosed in the male consultation in the infertility unit at Kut Hospital, Wasit Governorate, were retrospectively analyzed in the IVF Center from February 2022 to October [3]. Male patients suffering from infertility were taken and we drew blood from them for analysis. karyotype Chromosome. Males who were unable to achieve pregnancy despite regular intercourse with their wives

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who had been married for at least a year but were unable to achieve it. were also identified as suffering from infertility,in this study, we found that male patients suffering from infertility had a good quantity and normal activity of sperm. After careful examination and After that, we excluded other causes that could cause infertility. Semen was taken from male patients who suffer from infertility and was thoroughly examined, where seven male patients, who did not have sperm in their semen and physical examinations were performed on them, were diagnosed with what is called non-obstructive azoospermia. Also in this study, we found that azoospermia indicates non-obstructive azoospermia in some male patients. Male patients who suffer from low sperm concentration in the semen and less than 32% movement in the progressive movement of sperm. These male patients are diagnosed with azoospermia and low motility. All procedures undertaken for the purpose of the study were informed to the patients and their consents were taken in within the ethics of scientific research at Al-Kut Hospital in Iraq [4].

karyotype Chromosome analysis. Using the G banding technique, chromosome karyotype analysis was performed. Samples of peripheral blood were collected and taken, after which we cultured the lymphocytes on media with bovine serum (rpmi) 1640 for seventy-two hr. The cells were was harveste after being treated and purified with demicolcin for two hours and fifty minutes. The G band showed more than twenty metaphase chromosomes of each male patient. disorders chromosomal are also described and named with to the International System of Human Cytogenetic Nomenclature [5].

Measurement of serum hormones sex. The blood samples were collected by venipuncture. The blood was taken and placed in test tubes and left at room temperature to allow it to clot before centrifugation. The serum is then separated, preserved, and stored at -20 degrees Celsius for the purpose of testing. Then, the levels of several human hormones, including follicle-stimulating hormone (FSH), human (LH), luteinizing hormone, testosterone, estradiol, progesterone, and prolactin, are measured using a chemist's device (Roche) [6].

Statistical analysis. In this study, (graph-pad/prism) (5.0) software (Baghdad, Iraq) were use to analysis the data. Different between 2 or more groups were analysis using one-way analysis of variance with Tukey's test. Where age is presented as the mean ± standard deviation. Most data are presented as mean ± standard error of the mean; Statistical significance was set at (P 0.001) [7].

3. Results

Chromosome karyotype analysis. Data were collected on two hundred and five infertile male patients, one hundred twenty-five azoospermia male patients, and fifty-three oligozoospermia male patients for karyotype chromosome examination. The percentages were not within normal limits for male patients with infertility, azoospermia, and oligospermia (7%)%, (23.0%)%, and (15.01%)%. As found in Table 1, the abnormal karyotypes number in male patients with azoospermia were significantly higher than in those of infertility and oligospermia.

Table 1. Karyotypes (Abnormal) in different types of men infertility.

Infertility(Types)	Patients (number)	karyotypes (Abnormal)
Men Infertility N = 245	1 (7.0)%	(46,xy)inv11 ,(q23; q22.2)
	(2)	(46,x,y) ,qh
	(1)	(46,x,) inv(y),(p12q12)
	(1)	(46,xy),d l22, (p12)
	(3)	(46,xy) inv(5)(p12q14)
	(2)	(46,x)inv(Y)(p13Q15)
	(1)	(45,x)13/46,x,yQH-[75]
	(1)	(46,x)yqH+,inv(8)(p10Q12)
	(1)	(46,x) yQH-
	(1)	(46,y)1qH+
	(1)	(45,xy)Der(12; 22)(q11; Q11)
	(1)	(47,xxy)
	(1)	(45,xy)der(Q12; Q13)
	(1)	(46,xy),inv(9)(p11q13)
PN. Azoospermia N = 125	1 (23.0)%	(46,xy)qh-
	(17)	(47,xxy)
	(1)	(46,x,y) (8)(p13q11)
	(1)	(46,xy)t(1; 4)(q43; q20)
	(2)	(46,xy)1qH+
	(1)	(46,xxy)der(11; 20)(Q11; q11)
	(1)	(46,xy)16pS+
	(1)	(46,xy)inv(11)(p10; Q11)
	(1)	(47,x,y)qh-,+mar[61]/46,x,yqH
	(1)	(45,x) 23/46,x,yqh-[73]
	(1)	(47,xxy)(14pstk
	(1)	(47,x,y)qh [61]/46,x,yqh-33
	(1)	(45,x) 23/46,x,yqh-77
PN.Oligoasthenospermia N= 53	1 (15.01)%	(47,xy) 97 /46,xy[5]
	(2)	(46,xy)1qh+
	(2)	(46,y)inv 7 (p11q11)
	(1)	(46,xy)ch+g(14)(21) (46,xy)del(12)(q21)
	(1)	(46,y) q11; q22
	(1)	(46,x)yqh-

Male patients have most common types of chromose abnormal of infertility were peripheral chromosome inversion (9), with an incidence of 17.6 percent (3/17). A circumferential inversion of chromosome 9 has also been shown in male of oligospermia. The incidence of Klinefelter syndrome (47,XXY) were 60.71 percent (17/28) in male patients of azoospermia and an abnormal karyotype. Also polymorphism 46(XY,1qh+) was showen in all group. Detail is given in Table 1 .

Hormone abnormalities in different types of male infertility. We also data collected on men hormone levels in ninety-seven azoospermic male patients showing normal karyotypes (mean age, 31.40 ± 5.40 years; range, 17-88 years), and twenty-eight azoospermic men showing Ten infertile male patients showed abnormal karyotypes (mean age, 33.92 ± 7.00 years; range, 25 -46 years), and 54 healthy volunteers with normal physical examination findings served as a control group (mean age, 31.91) ± 8.29 years, (18-53)

years. Since not differences was identified in levels of estradiol, progesterone, or prolactin between the 4 groups. The testosterone level in male patients with azoospermia who found karyotypes abnormal was significantly low than in the other study groups ($P < 0.0001$). However, serum FSH and LH hormones levels was significantly more than in azoospermic men showing karyotypes abnormal compare with the other control and groups [8].

4. Discussion

Chromosomal abnormal and hormone male levels difference between differented types of infertile male in this study. Also showen that Klinefelter syndrome is the most type common of chromosomal aneuploidy in male patients of azoospermia. What we also found is that (XXY) syndrome was the only chromosomal abnormal in which a large percentage (about 50) percent of cases arise as a results with non disjunction in the paternal first meiotic divisions [9]. The incidence with klinefelter syndrome were percent among male patients with of azoospermia (non obstruction), which is slightly higher than the percentage (9.00)percent to (11.22) percent mentioned in [10,11].

The mechanism genetic of men infertil is still uncertain, although all or many study have focused on searching for the causes of hereditary infertility. Many researchers have worked to study and evaluate chromosomal abnormalities and have also studied and evaluated mutations in genes associated with infertility. An example is where known genes in testis (tex 11 and tex15, respectively) in meiotic recombination play crucial roles., chromosomal synapsis, and gametogenesis in males [12,13].

Due to a defect in the pituitary gland and testicles, In infertile men, hormonal disorders occur, and characterizing the hormonal causes of infertility in male patients is an important factor for the purposes of treatment and diagnosis. The male hormone testosterone inside the testicle is a very important factor in maintaining the formation and production of sperm. At the recant study, 29% of urology report that the use of synthetic exogenous testosterone to treated low levels testosterone hormones in male patients infertility [14,15].

FSH and LH are hormones secreted and synthesized by gonadotropin cells in the pituitary gland(anterior). In men , the combination of the hormones LH and FSH stimulates the producted of testosterone hormone by cells called(Leydig cells) in the testicle, and also enhances sperm formation [16,17]. The just so role of FSH in the producted of the male hormone testosterone in men is not entir clear. Decreased testosterone levels or eleveated LH levels have been found in an estimate 26% - 33% of patient of men infertile [18]. The effected of LH hormon stimulate spermatogenesis within the testicle is through mediate testosterone [19]. By means of testosterone, it is possible to inhibit release with the hormones FSH and LH hormones in gonadotropin cell, and ultimately leading to inhibition of spermatogenesis. In this study, male patients with azoospermia who showed abnormal karyotypes high testosterone levels, while LH and FSH levels were Most often, an abnormal karyotype can be detected in men with azoospermia, if there is decrease testosterone and increas LH and FSH.

The women sex hormone is estradiol, which is the primary responsible for the development of females and the the stability and preservation of secondary sexual characteristics. Such as the hormone progesterone, which is an steroid that participates in pregnancy, cycle, and human embryogene. the prolactin hormone is It also has a role in helping females produce the prolactin hormone (the milk hormone). The physiological levels of the hormone prolactin in males enhance and strengthen the LH receptors in the Leydig cells in the testicle. This leads to the secretion of testosterone, which further affects the formation of men's sperm inside the testicle. Whereas the study showed that there were no statistically significant difference in the rate of progesterone, , prolactin, and estradiol

between the 4 groups. This study and research It can be an auxiliary reference in treating cases of delayed childbearing.

5. Conclusion

This study highlights the critical association between azoospermia and chromosomal abnormalities, particularly Klinefelter syndrome (47XXY), in infertile male patients. The elevated levels of FSH and LH hormones combined with lower testosterone levels observed in these patients underscore the importance of hormonal evaluations in diagnosing male infertility. The chromosomal analysis, alongside hormonal profiling, provides valuable insights that can inform genetic counseling and the development of reproductive technologies.

The findings suggest that a comprehensive approach involving both genetic and endocrine evaluations is essential for understanding the underlying causes of male infertility and for developing effective treatment strategies. Future research should continue to explore the genetic and hormonal dimensions of male infertility to improve diagnostic accuracy and therapeutic outcomes.

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