Review Article: Androgen Hormone and Male Infertility

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ABSTRACT
Infertility, the inability to conceive after 1 year of unprotected intercourse. There are controversial studies about the factors that affect male fertility, the more prominent risky lifestyle influences such as cigarette smoke and consuming alcohol, the present research examined the possible implications of these observations behaviors about sperm genesis, human reproductive hormone, and oxidative profile of blood plasma. Male infertility is a reproductive health condition that arises worldwide as a severe medical and social challenge that affects the affected couples' heavy trauma, mental distress, and psychological stress. Males are confirmed to be the primary causative factor in 50% of the diagnosed cases of infertility. Male infertility may be measured by sperm cell content and quantities, as well as by structure. A description of a wide variety of factors responsible for male infertility is given in the current study. The primary causes are hormonal imbalances, developmental anomalies, physiological & morphological genital disorders, sensitivity to contaminants & pollutants, reactive oxygen species, and smoking. Besides, noise, changing habits, lack of adequate nutrition and diet, addictions, infections, drugs, diseases, and psychiatric issues can often lead to infertility problems that may impact the male reproductive system temporarily or permanently.

Keywords: sperm genesis, male infertility, hormonal imbalances, male reproductive system.

I. INTRODUCTION
It is possible to describe infertility as an organic goods failure to accomplish pregnancy after a year, or a year, with uncontrolled nuptial exposure. In the male case, if they do not impregnate their partner after one year of unprotected sex, a man is said to be infertile. Male infertility may appear in conjunction with other complicated disorders or syndromes and as an individual condition.[1]

50-80 million persons have infertility on a worldwide scale. About 8-10% of couples are estimated to suffer from this issue by the World Health Organization (WHO). Many experiments have shown that semen development and male fertility have declined in many countries worldwide during the last decades. However, in sperm count and semen content, the various regional areas vary.

These variations have also been verified by research from disparate nations. Men from the West, compared to Men from the East, have low semen content with a higher chance of testicular Cancer-Swedish, Finnish and Estonian. Eastern European countries have also recorded decreases in infertility. Other region, India, also reports a reduction in fertility, decreasing sperm counts. A new study on India's infertility that says approximately 50 percent of men's falsehood is linked with male fertility defects or complications. Over recent decades, this decline in fertility implies altered lifestyle, emissions, foods dependent on pesticides, lack of nutrients, tension, attributes to infertility to any degree of deskbound employment. Growing industrialization and civilization, which adds toxic pollutants, contaminants, and electromagnetic waves to the atmosphere that often influence other variables that lead to reproductive disorders, is the most frequently attributed cause. Several idiopathic infertility cases, such as chromosome aberration, microdeletion, and mutation, have a hereditary origin.[2-5]

The development of ROS (Reactive Oxygen Species) and, therefore, spermatozoa apoptosis also occurs in infertility cases due to the influence of multiple causative factors, such as cocaine consumption and smoking, resulting in apoptotic cell death of red blood cells and ultimately triggering endanger to sperm genetic code in diverse manners. Both trigger factors cause result in lowered sperm sustain abilities, trike, morphological method, concentration, and various types of reproductive organ disorders that directly tend to cause psychological illness and, finally, sterility. Most of these organic goods variables may be detected and resolved by medical treatment, although a few instances are not known and eluded to an inconsistent infertility.
Figure 1: Possible mechanisms of inflammation mediated ROS in male reproductive organs

Antiestrogen, carnitine and trace gonadotrophins components can help boost the quality of sperm. Sexual and reproductive wellbeing may be impaired by abnormalities of the epididymis' role, i.e., semen and seminal fluids in the penile urethra are ejaculated and erected. A significant factor/contributor to male infertility can be erectile dysfunction (incapacity to maintain a prolonged erection). Through clarifying the condition fundamental gene editing origin it has infertile phenotypes, that could be necessary with classify triggers of miscarriage and fertility assess the successful treatment. Many papers have been published on multiple factors responsible for male infertility. [6-7]

Therefore, this analysis has summarized many large and slight formative periods and its impact on the fertility of males.

II. SEMEN EFFICIENCY AND QUANTITY

One of the most restrictive systems is sperm cell morphology. The willingness of the sperm to replant sufficient ovaries for its intent is regarded as the supreme prerequisite. The sperm quality and amounts inside the semen are directly related to male infertility. The success of mating depends on the quantity and semen amount provided from the woman and the capacity for the sperm for hitting the fertilization place or position the capabilities of the sperm fertilizer to perform phase 21 fertilization. The content or quantity from semen formed and sperm ejaculation abnormalities are implicated in sperm defects. More than 90 percent from semen formed and sperm ejaculate abnormalities are implicated in sperm defects. More than 90 percent from semen formed and sperm ejaculation abnormalities are implicated in sperm defects. More than 90 percent of pregnancy for males cases are 22, owing to high semen values, and harmful sperm content.

Numerous causes, varying from congenital disabilities and hereditary conditions to dietary patterns and environmental pollution, may cause sperm abnormalities. The reasons for sperm defects remain unclear in several instances. Sperm durability can be calculated by sperm tail membrane oxygenation, fertility, development, morphology, and dignity. About 2.6 ml to 5 ml is the normal semen amount per ejaculate, with a requirement for 21.1 million sperm, semen per ml to affect fertilization and accomplish conception [8].

Although fluctuating semen concentration, depending on the causal factor, it may be transient or irreversible. However, sperm requirements have recently been reassessed. Lower characteristics of semen and sperm reference points have been identified through the Specific, retrospective, productive testing males, described as males whose wife Conceptualized during 1 year for contraception being discontinued.

In Azoospermia Factor (AZF) region, for rhabdomyolysis and 13 percent damaged azoospermia of spermatozoa are usually associated with Y chromosome- Y chromosome microdeletion defects. It is also possible that any morphological shift in sperm would have detrimental consequences its functional features quality. Empirical data shows that the double Faced sperm, tail-deficient sperm or abnormal wish to discuss, or some such morphological formulation abnormalities cannot engage in the process of fertilization. Other infertility forms include morphological sperm abnormality (teratozoospermia) and low motility of sperm (asthenozoospermia). A mixture of these can also occur, the most typical of oligoasthenoteratozoospermia (OAT) [9]. About 30% of infertile OAT males are successfully treated with idiopathic Infection.

Idiopathic oligoasthenoteratozoospermia (IOAT) with unknown aetiology is characterised as impaired spermatogenesis and is found to be undetectable by normal laboratory methods. Immune negotiator mastic cells are reported in a theoretically reversible way to specifically inhibit sperm motility and may be a widespread pathophysiological mechanism for many infertility-responsible factors. Either of the characteristics
or combinations listed below result in unusual changes in the quality and quantity of semen and sperm. The reasoning behind the particular unexpected explanation for this is that the words used to identify anomalies of semen research have conflicting interpretations and are sometimes misinterpreted and need improved scientific technologies; the best approach to dump these dark and confusing marks is to document semen analysis quantitatively.

III. DISRUPTION OF HORMONES AND HORMONAL IMBALANCE

Male infertility is associated with hypogonadism, ineffective levels of sex steroid hormones. The presentation of hypogonadism depends on the age of onset and the degree of testosterone deficiency\(^{[10]}\). Variations in presentation include ambiguous genitalia, delayed puberty, postpubertal gonadal failure, gynecomastia, impotency, and infertility.

Androgens play a crucial role in the development of male reproductive organs such as the epididymis, vas deferens, seminal vesicle, prostate and the penis. Furthermore, androgens are needed for puberty, male fertility and male sexual function. High levels of intratesticular testosterone, secreted by the Leydig cells, are necessary for spermatogenesis.

In the growth, development, metabolism, and reproduction of vertebrates, hormones play a large and central role. Hormones improve homoeostasis via the management and synchronization of complex bodies functions\(^{[11]}\). The TDS (Testicular Dysgenesis Syndrome) is a cardiomyopathy retardation of the framework and activity of the seminiferous tubules, inextricably connected to the undue accumulation of sex hormones at certain stages in the development cycle, which leads for masculine fertility. The Hormonal variables operate in a mutually integrating connection with a personality effect along one way to their output and secretion rates.

Current academics have suggested that spermatogenesis can be suppressed by copious amounts of circulating estrogens and adversely influence the power of male fertility. The tumors of germ cells develop β-HCG and alpha-fetoprotein. Increased β-HCG levels of intratesticular estradiol development decrease or hinder in the post-antibodies lysis. Sperm production high AFP levels decrease complete country oozoospermia of sperm. Besides, patients with germ cell tumors have been shown to have increased serum follicle-stimulating hormone (FSH) levels, an unusual source of treatable male infertility.

There was a detailed medical history and physical assessment for each subject. One of the authors performed in-person interviews with research participants. Detailed details on demographic characteristics (ethnicity, education, weight, height, and occupational status), reproductive background, history of previous medical and surgical disorders, exogenous hormone usage, physical activity, and tobacco and alcohol use was obtained using a self-administered questionnaire. Each patient's body mass index (BMI), measured as weight (kg)/height\(^2\) (m)\(^2\)\(^{[12]}\). The location and existence of the measurements were included in the urogenital study, with the testicular volume measured using ultrasonography. It was deemed tiny to have a volume of less than 12 ml. Blood was obtained for the assessment of serum luteinizing hormone (LH), follicle stimulating hormone (FSH), compleat testosterone (T), free testosterone (T-free), prolactin (PRL), estradiol (E2), free estradiol (E2-free), SHBG, thyroid stimulating hormone (TSH), thyroxine (T4), triiodothyronine (T3), and amounts of inhibin B after overnight fasting. Analyses were also conducted on haematological and routine biochemistry. At least two semen tests after 3 days of abstinence with an interval of 4 weeks between them were also included in the laboratory evaluation, Karyotype analysis and Y chromosome microdeletion assessment. The existence of antisperm antibodies was also calculated using the Mixed Agglutination Reaction (MAR) test of antibodies.

No preventive steps have yet been tested for obesity-associated male infertility. Thus, to recognize its function and care, greater clinical understanding is needed.

Receptor deficiency and biosignalling pathway defects also lead to the issue of male infertility. In some instances, dysfunctional receptors that mediate the biosignalling pathway of sex steroids influence male gonadal organs' growth and organization. Optimal interaction between different hormonal factors, especially testosterone, is necessary for male sex organs' development\(^{[13]}\). The Male gender hormones work in a predefined way, i.e. dopamine, and are regulated by a cytosolic receptor in the target cell. Testosterone's action should not be controlled by a faulty receptor, resulting in the creation of the medical disorder defined as feminization of the testicles Insensitivity to androgen, which could be deemed the source of infertility for males. Unproductive androgen and FSH signalling cannot reply to an endogenous biological signal, including a clinical trial, environment that induces spermatogenesis and could be responsible for infantile primate testicular azoospermia.

IV. ABNORMALITIES IN ANATOMY

Testicular or post-testicular abolishment of reproduction could be induced by numerous conditions in various male reproductive organs. In developing nations, a syndrome known as cryptorchidism is one of the prominent anatomical anomalies linked with male infertility, impacting 2-4 percent of male babies, most often in premature infants. Testicles refuse to descend until birth through scrotal sacs in this state. Abdominal testicles cannot assist the spermatogenesis mechanism since it needs for sperm cells to grow into healthy.
mature, and fertilizable sperm, a temperature (2°C) below the average temperature of the human body.

The specific trigger of cryptorchidism, however, remains unclear. The emergence and increased occurrence of cryptorchidism can be aided by different causes, primarily hormonal, genetic, and environmental factors. This raises the factor of danger for decreased fertility and rectal cancer (33 percent to 66 percent), which is 5-10 times greater than average. Defects clarified a minor cause for cryptorchidism in the Factor 3 gene-like insulin, it’s roger, and plasminogen activator genotype. The study was given in favor of the intraterine climate and maternal descent, leading to the cryptorchidism phenomena.

Although long term rehabilitation is still in its infancy, surgical care is still in its infancy with orchiopexy species to retain spermatogonia 35 is prescribed between 6 and 12 months. The possibility of subfertility or malignancy can be minimized by early surgical therapy. After 12 years of age or without orchiopexy, patients experiencing orchiopexy have a 2 to 6 fold change of having testicular cancer relative to those undergoing testicular cancer between the ages of 10 and 12\(^{15}\). But, owing to the substantial difference in pathogenesis, hypospadias is not closely correlated with cryptorchidism.

Chromosomal defects have been identified in patients with cryptorchidism and hypospadias. One more irregularity, varicocele, is a series with vas deferens arteries unnaturally having contractions that discharge the testisculum. This could happen on all sides of the, still but it’s more popular on the left side. Around 15 percent of all adult males are found to have clinical varicocele. Varicocele can decrease the quality and volume of semen, and sometimes testicles may shorten. Besides, male infertility can lead to epididymitis, the vesicular universal disorders, infection and tubular harm/dysfunction due to infection. Congenital abnormalities in the proximal portion of the vas deferens can be either infrequent, with a regional deficiency, or with inclusive irregular growth.

V. OCCUPATIONAL/CHEMICAL EXPOSURE

In the developing world, economic research reflects on the ideas of conspicuous consumerism, techniques of industrial manufacturing, ever-expanding technical structures, and growing developments in chemical cultivation, which have introduced citizens to countless amounts of chemicals that have not been considered for decades\(^{16}\). There are many chemicals that, either by modifying spermatogenesis, sperm parameters, or hormonal dysfunction, may affect men’s fertility momentarily or permanently. Chemical occupational exposure sufferers that are receiving care for infertility can often may linked by this problem of infertility. Among such chemicals are lead, diamino stilbene, benzo(a) pyrene (BaP), dibromo chloropropane and carbon disulphide.

The probability of infertility can be marginally enhanced by prenatal diethylstilbestrol (DES) exposure doesn’t really, nor does not impact amount childbirths of fathers or actual births. By causing oxidative stress, sulfa salazine can induce male infertility. Among heavy metals, the antifertility effect of lead was first identified. Strong lead and cadmium toxicity can reduce the efficiency of semen. Oligoteratozoospermia and asthenozoospermia can result from exposure to copper. In human tests, semen content declines were found in welders subjected to chromium. The spermatogenesis impact of the nematocide dibromodichloropropane (DBCP) is negative. Owing to the absence of plasma testosterone level, ethane 1,2-Dimetane sulphonate (EDS) induces Leydig cell toxicity\(^{17}\). Often, sodium bicarbonate is a sexual potent toxin compounds that lowers amount of oestrogen inside. By increasing oxidative stress, chromium compounds specifically cause harm to testicular tissue. Aluminum contributes to decreased reproductive organ weight and impairs fertility. The harmful substances recorded on breeding and fertility of chloride million Americans live.

Several pesticides, especially POP (Persistent Organic Pollutants), i.e., non-metallic un biodegradable and dont des, are severe invited for an interview for reproduction that are organic goodsly magnified upon entering the food chain and causing severe issues, like reproductive toxicity and infertility, in the human system. Dose-dependent, 1,2-dibromo-3-chloropropane (DBCP) induces decreased fertility by influencing post-testicular sperm via the process of reduction of C\(_5\)H\(_6\)O\(_2\)-to-CO\(_2\) metabolism through epididymal Sperm cells defeated.

Exposures to OP (organophosphorus) with higher sensitivity, it could be necessary for DNA denatured proteins to modify human sperm chromatin condensation and can adversely affect the reproductive system through the protein phosphorylation mechanism \(^{18}\). Although the fundamental cause for the irregularity of the estrogen sex steroid mechanism by antiandrogenic pesticides, it is not obvious, and it may serve as an inhibitor of five alpha-reductase, which may interfere with the endocrine system.

VI. POSSIBLE INFLAMMATION-MEDIATED PATHWAYS OF ROS IN MALE REPRODUCTIVE ORGANS

O\(_2\)\(_2\), which seems to play a part in this phase, is the primary ROS produced in hematopoietic cells. There have been reports of capacitating populations of mammalian spermatozoa that develop ROS mainly through two mechanisms. With consistent digestion, the mitochondria located in the mid-piece region of the sperm develop a low degree of ROS. O\(_2\)\(_2\) formed from these two sources is presumed to mix with NO in LPS-treated, the elevated testicular amounts of MDA and NO could be
attributed to the possibility that released inflammatory mediators join the local phase independently and exacerbate the redox imbalance. The extent of the relationship between toxic oxygen metabolites and cell macromolecules is calculated by the Redox imbalance, which ultimately influences the fertilizing capacity of germ cells.

**Lifestyle, Causes of Nutrition & Diet**

A variety of lifestyle variables that may negatively influence male fertility have been proposed in recent years. Insufficient and imbalanced lifestyles may help the possibility of impotence in men. Male fertility can be adversely impacted by deskbound jobs, tight clothes, diet composition, and holding cell phones near to the scrotum. Over recent decades, the reduced content of human semen can be attributed to either a shift living through living patterns, demonstrated bound by more workstations jobs with proven capabilities consumption and a growing rate of diabetes. This is also unknown, though, who are these guys variables directly impact them. In order to create a definitive connection between lifestyle variables and the occurrence of infertility among males, more studies are needed.

During spermatogenesis, reduced GSHr levels suggested a lack of cohesion of spermatozoa integrity, resulting in oxidative stress. GSH is vital for the sperm scavenging mechanism and necessary for the creation of glutathione peroxidase (GPX4) phospholipid hydroperoxide, which is present in spermatids and is essential for the formulation of the protein needed for the development of the sperm mid-piece. The absence of either material may contribute to mid-piece deformation and motility malfunction. Besides, the inhibition of sperm peroxidation may be responsible for GPx and GSH reductase. Similarly, smoking and alcohol intake often inhibit the expression of Nrf2, which has a defensive function against oxidative harmful effect(fig. 2).

**Figure 2: Likely intracellular oxidative mechanisms in spermatozoa**

**VII. POSSIBLE OXIDATIVE INTRACELLULAR PATHWAYS IN SPERMATOZOA**

(a) It is suspected that oxidative stress is implicated in the production of ADHD in humans, cancer, Parkinson's disease, Lataora's disease, Alzheimer's disease, atherosclerosis, heart failure, myocardial infarction, fragile X syndrome, sickle-cell disease, lichen planus, autism, infection, chronic fatigue syndrome (ME/CFS), and depression.

(b) The male type of gametocytogenesis is spermatocytogenesis which results in the development of spermatocytes containing half the usual genetic material complement. Diploid spermatogonium, which lives in the basal compartment of the seminiferous tubules, divides mitotically in spermatocytogenesis, creating two intermediate diploid cells called primary spermatocytes. Each primary spermatocyte then moves into the seminiferous tubules' adluminal compartment and duplicates its DNA and subsequently undergoes meiosis I to create two secondary haploid spermatocytes, which are subsequently divided into haploid spermatozoids again. This distinction includes genetic diversity origins, such as spontaneous addition of either paternal chromosomes or chromosomal crossover, which enhances the gamete's genetic heterogeneity. In spermatogenesis, the DNA damage response (DDR) machinery plays a significant
function. The protein FMRP attaches to meiotic chromosomes and, during spermatogenesis, controls the dynamics of the DDR machinery. FMRP appears to be essential for DNA damage repair.

Marsellus et al. have found that the nicotine compound in a cigarette can impair ethanol enzymes' synthesis in the body. The combination of ethanol and nicotine can induce excessive ROS output compared to ethanol or nicotine alone[21]. This report confirms our results more in infertile men than smoking or alcohol consumption alone about the combined usage of smoking and alcohol use impaired antioxidant status.

Pollution and radiation: human beings are influenced by various kinds of pollution such as air, water, dirt, vibration, and nuclear, creating harmful consequences on their body organs and thereby contributing to severe diseases. Air contamination, two to three months after exposure, is related to decreased sperm motility. Approximately 50% of the production of estrogen receptor with sex steroids (ER-alpha) in TM3 mouse Leydig cells is blocked by diesel exhaust particles (DEP).

Illnesses:

The cause of infertility in around 14 percent of men who are infertile is a total shortage of sperm. If a man does not contain semen, azoospermaia is named (pronounced ay-zoh-uh-SPUR-mee-uh). Azoospermaia may be induced by a hormonal deficiency or a blockage in sperm flow.

A man develops fewer sperm than average in certain instances of infertility. This disease is termed oligospermaia or a reduced sperm count (pronounced OL-ih-goh-SPUR-mee-uh). Varicocele (pronounced VAR-ih-koh-seel), a swollen vein in the testicle, is the most frequent source of oligospermaia[22].

Different locations of the male reproductive tract, such as the testis, epididymis and male accessory sex glands, and spermatozoa, can be impaired to varying development, maturation, and transport stages. Spermatogenesis can exacerbate the infectious process, affect sperm function, and obstruct the seminal tract. 

Drugs:

Experiments have found that, since they can cause miscarriage, certain medications used to cure certain illnesses are harmful to reproductive health. High blood pressure management medications[23], antidepressants, CNS depressants, and drugs used to manage gastric issues that conflict with sperm development and ejaculation are several examples of prescription drugs that may contribute to male infertility. For hypertension patients, a category of drugs-calcium channel blockers (CCB) is usually administered as they improve blood and O2 flow to the heart, helping to reduce its function. However, by stopping the sperm from penetrating an embryo, they interfere with the fertilization process and are generally correlated including infertility for males[24]. Lengthy ownership of those medications suppresses spermatogenesis as cytoplasmic calcium controls certain sperm functions, such as motility, hyperactivity, acrosome reaction, and capacitation. The impact of the CCBs on removed medication is reversed. 

Antibiotics:

The most of the drugs that influence sperm can limit development, creating a low sperm count, although some others will affect the way the sperm works. Low sperm counts indicate that the spouse would have less sperm sufficient to fertilize an embryo, and if the motility of the sperm[25] (its capacity to move) is diminished, it would be harder for the sperm to enter the egg.

Depending on the drug, how long a treatment controls the sperm of a man depends. A decent rule of thumb is that a man does not expect any improvements to arise before the drug is stopped for at least two to three months. That's because to develop and completely grow, it takes sperm almost that long. So what he's done in the past 90 days will impact his semen (or the kid he makes) now, such as consuming recreational substances[26]. And what he's done now, two or three months from now, would turn up in his semen.

VIII. CONCLUSION

A wide variety of variables and causes lead to male infertility’s growth and progression. Overall, reproductive disorders are typically caused by the overall condition of one’s wellbeing. It is more likely that men who live a healthier lifestyle develop healthy semen. Many reasons responsible for male infertility have been revealed in the present study. Some incidents are attributed to physiological anomalies such as cryptorchidism, hormonal deficiency, and hereditary disorders. Still, human beings are liable for specific causes themselves, such as adverse reactions to the climate, erratic lifestyles, poor nutrition, and alcohol and cigarette abuse. A few early experiments have focused on the influence with free reactionaries on male fertility phytonutrients as well as function. While several choices for therapy are open, medications sometimes do not function. Therefore, human exposure to hazardous chemical agents, chemicals, fertilizers, narcotics, radiation, traumatic consumption habits etc. which contribute significantly in infertility, must be limited. There are some species that are often recorded producing detrimental impacts on the reproductive organs and the above causes. Future studies can also investigate in all influences, including animals, harmful effects and medications, and it is essential to explain the comprehensive process of their action. Governments worldwide should develop progressive policies to phase out the manufacturing, usage, and storage of dangerous chemicals. The Scope (Registration Assessment and Authorisation of Chemicals) the rules floated through the EU is a sign of welcome in this sense. Addressing male infertility issues, a sound and educated public opinion must eventually be established.
REFERENCES


