

Risk Factors and Causes of Male Infertility-A Review

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Abstract

Infertility is defined as inability to achieve conception in a period of one year in a couple, despite regular and adequate unprotected sexual intercourse. A male is said to be infertile if he is unable to impregnate his partner after one year of unprotected intercourse. It is an important medical and social problem in the world as regards 15% of couples are infertile and 40% are infertile because of male factor infertility. This review highlights the risk factors and some causes that are responsible for male infertility. The aim of this review is to generate information which could help in the evaluation of male infertility.

Keywords: Male infertility; Obesity; Smoking; Varicocele; Endocrinal disorders

Introduction

Following regular and frequent unprotected sexual intercourse, about 84% of couples in general population are expected to conceive within one year and about 92% should conceive within two years. When a couple fails to conceive even after two years of regular frequent coitus and there is no known reproductive pathology, the couple may be considered infertile [1]. However, the term infertility implies a definitive inability to conceive. Therefore, couples who do not conceive in more than one year should be regarded as sub-fertile. According to this definition, approximately 14% of the couples are sub-fertile. To be more exact, the term sub-fertile means a male who failed to conceive after one year of regular unprotected intercourse with the same partner and who had a sperm count of less than 20 million/ml [2]. Infertility has increased as a problem over the last thirty years all over the world, regarding to social phenomena, such as the tendency for marriage at a later age and child bearing, increasing use of contraception specially Intrauterine device and liberalized abortion [3].

The incidence of infertility in a population has important demographic and health implications [3]. The prevalence of infertility varies widely, being less in developed countries and more in developing countries where limited resources for investigation and treatment are available [4]. Infertility is an important medical and social problem in the world as regards 15% of couples are infertile and 40% are infertile because of male factor infertility and 40% are because of female factor infertility and in the remainder both factors are associated [5]. Infertility is a worldwide problem and approximately 8-10% of couples within reproductive age group are infertile. It is estimated that globally 60-80 million couples suffer from infertility every year, of which probably between 15-20 million are in India alone [6]. Infertility is a common gynaecological problem affecting 15% of couples attempting their first pregnancy, in which cases it is called primary infertility;

while those with secondary infertility are about 10% of the population. Secondary infertility could be as high as 52% in some sub-Saharan African countries and as low as 23% in some Asian countries [7].

Risk Factors of Male Infertility

Age

Blood testosterone levels decline with age in most men, even in those who are healthy, and this decline probably begins around the age of thirty [8]. The decline of around 1% per year in testosterone levels after the age of 30 years has been termed the andropause [9]. However, a more technically accurate description for the decline in testosterone might be "symptomatic hypogonadism in aging males." Hypogonadism is not defined by any specific level of serum androgens because the testosterone level that causes dysfunction varies widely among individuals [10]. The symptoms associated with symptomatic hypogonadism in aging males include decreased libido, decreased muscle mass, decreased bone mineral density, increased fat mass, central obesity, insulin resistance, emotional irritability, dysphoria and erectile dysfunction [11]. The risk of becoming infertile doubled in men who are over 35 years old compared with men who are under 25 years old, and five times longer to conceive at the age of 45 years [11]. In a study on a convenient sample of fifty five healthy men ranging in age from 52 to 79 years old compared with a control group of men less than 52 years old found that older men had lower semen volume, with abnormal sperm morphology and reduced vitality [12]. A study in Belgium by Mahmoud et al. showed that testicular volume of elderly males in their eighth decade was significantly less with 31% when compared with the young control group of 18 to 40 years old [13].

Smoking

Smoking can decrease male fertility by decreasing the sperm motility and percentage of normal sperm cells, and that a decrease in

the percentage of motility of sperm cells and normal morphology is correlated with the number of cigarettes smoked per day [14]. Smoking has also been linked with an increase in reactive oxygen species levels, leading to oxidative stress in the environment. This oxidative stress may exceed the antioxidant capacity of seminal plasma and can be toxic for sperm, causing oxidative damage [14]. One of the studies revealed that smoking leads to a decrease in semen parameters such as viability, sperm concentration, motility and morphology [15].

Obesity

Several studies have shown that fertility decreased in overweight and obese women [16,17]. Similarly, obesity may play a role in men fertility. A study in United State investigating farmers and their wives showed that 10 kg increase in the body weight may reduce fertility by nearly 10%, and the great effect for men with a body mass index (BMI) of more than 32 [18]. A significant reduction in the number of normal motile sperm has been observed among men with BMI over 25, it also found that men with excess fat in the thigh and suprapubic area have poor semen quality [19]. A Norwegian cohort study found that the risk of infertility is associated not only with high body mass index (BMI) but also with low BMI [20].

Occupational exposure

Among the factors thought to affect male infertility is the occupational exposure, it was found that there is no significant association between infertility and occupational exposure [21]. Another study conducted in Lebanon had demonstrated that occupational exposure to harmful physical and chemical agents is associated with increased risk of male infertility [22]. Exposure to organic solvents at work associated with reduction in count of motile sperm [23], a number of solvents that are used in industry may have an adverse effect on male reproductive function like carbon disulphide that had shown to affect semen quality but in low exposures had shown no effect [24]. Previous exposure to glycol ethers in work place associated with decrease in the semen quality [25]. Semen quality in workers exposed occupationally to hydrocarbons like toluene, benzene and xylene present anomalies, including alterations in viscosity, liquefaction capacity, sperm count, sperm motility, and the proportion of sperm with normal morphology compared with unexposed males [26]. Furthermore, welding may reduce the quality and quantity of semen, likewise, occupations in which the workers exposed to heat they have reduced sperm count. Also workers in agriculture or in a pesticide factory may experience a negative affect on reproduction, Dibromochloropropane can cause testicular toxicity and reduce sperm production. In men who exposed to Ethylene Di-Bromide had decreased sperm count and increase number of abnormal sperm, also insecticide have been found to have decreased sperm motility but there is no effect on fertility [25]. Dichlorodiphenyltrichloroethane is a type of pesticides can lead to decreased fertility and altered sperm counts [27]. Industrial and construction workers presents with an increase infertility rates because of greater exposure to stress [27], occupational stress was negatively correlated with the proportion of normal sperm [25]. Heavy metals like cadmium and lead reduce the quality of semen, mercury can concentrate in the testes beside other organs, mercury poisoning leads to infertility. Furthermore, mercury and copper can interfere in spermatogenesis [27].

Exercise

There are many health benefits of exercise, despite of that there are a conflict results about the effect of exercise on the male reproductive function. It was found that endurance training at highest level does not alter the male reproductive function, and there is no significant effect in hormonal profile and sperm parameters except for sperm motility in the cyclist (riding a bicycle) it was observed lower sperm motility but that may attributed to physical factors [28]. The effect of vicious cycling was studied in another study and it was found that infertility was from the less common symptoms [29]. But recent study suggesting that long term strenuous exercise have a deleterious effect on semen parameters [30], and also resistance exercise shows a significant decline in free and total testosterone [31].

Diet (Alcohol and caffeinated beverages)

Alcohol consumption affects the reproductive system at all levels [32]. Drinking caffeinated beverages may interfere with fertility in men; a study showed that men who consume more than three cups of tea daily is associated with decreased fertility [33].

Electronic devices

Exposure for a long time on a laptop will increase the scrotal temperature and have a negative impact on sperm parameters [34]. Furthermore, using cell phones has been noted to have an adverse effect on male fertility due to decreased semen quality which paralleled of daily exposure to cell phones [35]. Another study found that use of cell phones decreased the actual percentage of the live sperm and this correlated with the duration of using cell phones [36].

Stress

Most studies have rejected the theory of stress as the only factor in the etiology of infertility; but there is growing evidence to show that stress is an additional risk factor for infertile. Semen parameters are significantly decreased in men who are under stress [37]. Many forms of stress including psychological can affect male fertility and reproduction. The autonomic nervous system and the adrenal hormones participate in the classic stress response while also affecting the reproductive system [38].

Scrotal temperature

Types of undertrousers affect the scrotal temperature, and semen quality. Wearing tight fitting undertrousers is associated with increased scrotal temperature. Also the position or activity has its impact on increasing the scrotal temperature, walking is associated with significantly lower scrotal temperature than sitting [39]. Driving for more than two hours continuously is associated with increasing the scrotal temperature [40]. Spermatogenesis, especially differentiation and maturation of spermatocytes and spermatids, is temperature dependent requiring a temperature of at least 1°C to 28°C below core body temperature [41,42]. This is supported by studies in humans that artificially brought testicles near or into the inguinal canal and induced high scrotal and consequently testicular temperatures near core body temperature [43-46]. Consequently, spermatogenesis was impaired and semen quality reduced.

Reactive Oxygen Species (ROS)

Reactive oxygen species have negative effect on sperm parameter. The sperm plasma membrane is very sensitive to the effect of ROS since it contains abundant unsaturated fatty acids. The presence of high ROS levels in the semen implies an imbalance between ROS production and the antioxidant system. Increased ROS level can lead to damage with subsequent sperm dysfunction or cell death. These free radical or oxidative damage to sperm is thought to be responsible for many cases of idiopathic oligospermia. Men exposed to increased levels of sources of free radicals are much more likely to have abnormal sperm and sperm counts [47].

Therapeutic drugs

Primary infertility may result from the use of various drugs. This phenomenon may be the result of an effect on the hypothalamic-pituitary-gonadal axis or a direct toxic effect on the gonads. Some of the drugs are antineoplastic agents (cyclophosphamide, chlorambucil, busulphan, and methotrexate), glucocorticosteroids, hormonal steroids (diethylstilbestrol, medroxyprogesterone acetate, estrogen, and the constituents of oral contraceptives), antibiotics (sulfasalazine and cotrimoxazole), thyroid supplements, spironolactone, cimetidine, colchicine, marijuana, opiates, and neuroleptic agents [47].

Causes of Male Infertility

Varicocele

Varicocele is a dilation of testicular veins within pampiniform plexus of spermatic cord that holds up a man's testicles. Varicoceles are the leading correctable cause of infertility in men who present to an infertility clinic for evaluation [48]. According to human report update (2001) varicocele is found in 15% of general population including adolescents and adults [48] but the prevalence of varicocele among men attending the infertility clinics range between 30-40% [49]. Varicocele occurs most commonly on left side. The etiology of varicocele is multifactorial, the most common is the difference in the anatomy of the left and right spermatic vein, absence of valves in the spermatic vessels resulting in retrograde of blood flow and compression of the left renal vein causing a partial obstruction [50].

Endocrinal disorders

Endocrine causes of male infertility are often referred as pre-testicular causes. Impairment of fertility in these cases is secondary to either a hormone deficiency or an excess [51]. Hormonal disturbances are result in approximately 15% of married couples and males are responsible in about 50% of them. Fertility in men required normal functioning of the hypothalamus, pituitary glands and testes and the complete male germ cell development is dependent on the balanced endocrine secretion of these glands [52]. Abnormalities in hormone production may be a factor in male infertility. Hypogonadotropic hypogonadism which is the failure of pituitary gland to produce adequate amounts of follicle stimulating hormone and luteinizing hormone can lead to decreased sperm count and a state of infertility [53]. Hyperprolactinemia causes infertility in around 11% of oligospermic males. Hyperprolactinemia inhibits the pulsatile secretion of the gonadotrophin releasing hormone, which causes decreased pulsatile release of follicle stimulating hormone, luteinizing hormone and testosterone, which in turn causes spermatogenic arrest, impaired sperm motility and altered sperm quality. It later produces

secondary hypogonadism and infertility [54]. Since spermatogenesis occurs in close contact with the sertoli cells, the thyroid hormones must exert significant regulatory role in sperm production. Therefore disturbances in the thyroid function could affect spermatogenesis and male fertility [55].

Male reproductive tract infection

Infections of the male reproductive tract is a common disease that can deteriorate the quality of spermatozoa and impair the function of male accessory gland; for this reason it is considered one of the potentially correctable causes of male infertility. Infection of the male reproductive tract significantly decreases the levels of semen volume, α -glucosidase, fructose and zinc in seminal plasma suggesting impairment of the secretory function of the epididymis, seminal vesicles and prostate [56].

Ejaculatory disorders

Ejaculation consists of the coordinated deposition of semen into the prostatic urethra (emission), closure of bladder neck and contraction of the periurethral and pelvic floor muscles causing expulsion of the semen through the urethra (ejaculation). The process of ejaculation is dependent on central and peripheral nervous system control. Abnormalities of ejaculation can lead to lack of emission ejaculation and retrograde ejaculation and may be caused by neurologic, anatomic and psychologic conditions. Retrograde ejaculation is caused by incomplete closure of the bladder neck. Diabetes mellitus causes peripheral nervous system injury resulting in possible retrograde ejaculation or anejaculation. Central nervous system lesion such as spinal cord injury and myelodysplasia can also cause ejaculatory dysfunction. Some medications like α -blockers, antidepressants, antipsychotics and antihypertensive can also affect ejaculation. Anatomic causes of ejaculatory dysfunction include obstruction of ejaculatory ducts and prior surgery on the bladder neck leading to retrograde ejaculation [57].

Immunological factor

Antisperm antibodies are found in about 9-33% of infertile couple. In 8-19% of these couples, the antibodies are present in man and in 1-21% antisperm antibodies are contributed by the female partner. Risk factors for the formation of antisperm antibodies in man include vasectomy and epididymitis, although the exact cause for formation of antisperm antibodies is frequently unclear. Antisperm antibodies may decrease fertility potential at several critical points that are important to natural conception. They also cause sperm cells to agglutinate, hindering sperm motility. Sperm penetration through cervical mucus is also impaired. Sperm with antisperm antibodies also have poor sperm egg interactions. The acrosome reaction and zona pellucida binding may be impaired, which in turn may decrease overall fertility potential [57].

Genetic and chromosomal defects

Genetic causes account for 10-15% of severe male infertility, including chromosomal aberrations and single gene mutations [58]. A genetic disorder may alter spermatogenesis, impair normal development of the genital tract and decrease sperm motility and fertilization capacity, any of which may lead to varying degrees of male subfertility or infertility [57].

Unknown cause

Infertility of unknown origin includes unexplained male infertility and idiopathic male infertility; it is a condition in which fertility impairment occurs spontaneously or due to an obscure or unknown cause. Infertility of unknown origin accounts for 37% to 58%. Men classified as having idiopathic male infertility have an unexplained reduction in semen quality with no history associated with fertility problems and have normal findings on physical examination and endocrine laboratory testing [59]. The unexplained forms of male infertility may be caused by several factors, such as chronic stress, endocrine disruption due to environmental pollution, reactive oxygen species and genetic abnormalities [60].

Conclusion

There are various risk factors and causes that are responsible for infertility in males and these factors should be considered in the treatment of male infertility.

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