

Effects of lifestyle habits on fertility; practical recommendations for modification

Mathias Abiodun Emokpae¹, Somieye Imaobong Brown¹

¹ Department of Medical Laboratory Science, School of Basic Medical Sciences, University of Benin, Benin City, Nigeria.

Abstract

The role that lifestyle behaviors play on infertility issues has generated some amount of interest and questions amongst stakeholders. This review aims to highlight the impact of lifestyle behaviors on the fertility potential of an individual and what can be done to prevent or improve reproductive outcomes. Relevant published articles on the effect of lifestyle behaviors were obtained from several search engines for the study. The review of the literature indicates a negative impact of modifiable lifestyle habits such as obesity, fat-rich diets, psychosocial factors, sedentary lifestyle and alcohol and drug abuse were associated with fecundity. The ensuing stress precipitates social behaviors such as excessive alcohol and caffeine consumption, tobacco smoking, abuse of recreational drugs/medications, which increases the risk of sexually transmitted diseases and infection leading to infertility. Industrial activities leave the environment contaminated with toxic metals and chemicals which also affect reproduction. The religious beliefs and perception that children conceived through the Assisted Reproductive Technique are "artificial" is another serious issue to be dealt with. The need to make appropriate behavioral changes to stem the tide of infertility in Nigeria is imperative. More reproductive health education is needed to create the necessary awareness of the etiologies of infertility and the importance of in-vitro fertilization treatment as a means of conceiving 'natural' babies is suggested.

Disclaimer: The authors have no conflicts of interest.

Funding: Nil

J Reprod Biotechnol Fertil 9:41-58

Author contributions: MAE designed the study; MAE, SIB contributed in literature search; SIB drafted the manuscript; MAE wrote the final manuscript; MAE proofread the manuscript.

Correspondence: Emokpae, MA ORCID ID:0000-0002-6266-1774; email: mathias.emokpae@uniben.edu

Language compliance: This article was edited by the Australian Editorial Services (www.nativeenglisheditor.com)

Keywords: Behaviour, human, infertility, lifestyle.

Introduction

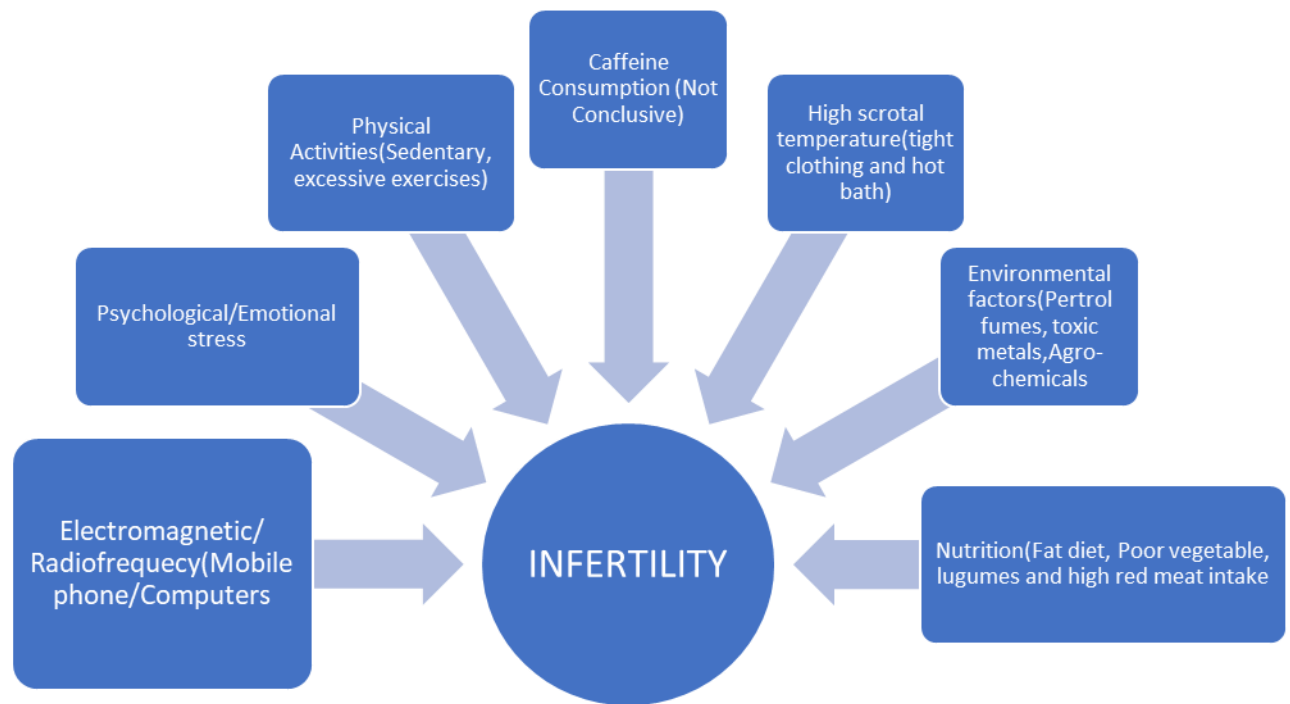
Reproduction is an important biologic event in humans as well as for all the living things and anything that threatens reproductive health will trigger a significant response from the scientific community since the continuous existence of any species is dependent upon the sound reproductive health of the parent species. There are reports which indicate that reproductive health has been deteriorating since the last 5-6 decades from different parts of the world especially in industrialized/developed countries as a result of environmental, occupational, and modern sedentary lifestyle factors (Kumar et al., 2018).

The role of lifestyle factors in the etiology of infertility has generated a growing interest among researchers. Several authors have provided evidence of an association between

lifestyle behaviors and infertility in both men and women, they include; delayed childbearing due to pursuit of career or education, age of starting a family, weight, smoking, alcohol and caffeine consumption, psychological stress, nutrition/diet, exercise, risk sexual behaviors, drug abuse, occupational risk factor, toxic metals, cellular phones and radiation among others (Araoye, 2003; Fehintola et al., 2017; Adewumi, 2017; Ilacqua et al., 2018; Damayanthi and Durairajanayagam, 2018; Silvestris et al., 2019; Emokpae and Chima, 2018; Ikyernum et al., 2019; Alabi, 2020) (Figure 1).

According to the World Health Organization, about 20-30% of couples worldwide are infertile, and up to 80 million women are affected by the condition; about 50% of all women in developing countries are infertile (Ombelet et al., 2008).

Figure 1: Schematic representation of lifestyle behaviors on infertility in both males and females



The prevalence of infertility in sub-Saharan African ranges between 20-40% and the problem is shared equally by both men and women (Uadia and Emokpae, 2015). It has been estimated that about one in six couples or approximately 15% of the population in industrially developed countries are affected (Sharma et al., 2013). Infertile couples suffer both emotional and psychological trauma due to pressure from family members and society. Fortunately, most of the causes of infertility are treatable with major procedures belonging to Assisted Reproductive Technology (ART) methods. However, the normalization of some modifiable lifestyle factors could restore normal oocyte maturation in women (Anderson et al., 2010) and improve semen quality in the males (Ilacqua et al., 2018). The understanding of the various mechanisms whereby modifiable lifestyle behaviors impair infertility in both males and females will go a long way to assist in the management of affected subjects. This review seeks to highlight the adverse effects of some lifestyle behaviors and suggests ways to optimize the infertile couple's chances of

obtaining conception and live a better quality of life.

Materials and Methods

A literature search was conducted using PubMed and Google search engines. A systematic review of relevant literature on the major lifestyle factors associated with both male and female infertility was performed.

Major lifestyle behaviors that may affect fertility

Lifestyle factors are obviously under the control of the individual and are modifiable to improve the wellbeing of humans. Lifestyle factors could affect reproductive health either positively or negatively (Homan et al., 2007; Ilacqua et al., 2018). Infertility can be defined as the absence of conception within one year of unprotected sexual intercourse, while fertility is the capability of producing an offspring (Aydin et al. 2014). The new trend of modern lifestyle is that people delay starting a family due to educational and career pursuit, such individuals

are older and fatter as a result of bad nutrition and a sedentary lifestyle, and they are stressed while trying to cope with the pace of this modern lifestyle. Consequently, they become alcoholics; tobacco intoxicated, and abuse illicit substances. These lifestyle behaviors expose one to the risk of infertility but because of the financial stability that comes with having a career; most believed they can afford assisted reproduction. The causes of infertility are varied ranging from endometriosis, ovulatory disorders, poor sperm quality, and unexplained conditions amongst others. Some authors suggested that adverse lifestyle factors such as smoking, alcohol consumption, excess body weight, and caffeine can have an additive effect on fertility. A study that examined couples who were trying to conceive naturally over 12 months, reported that only 38% couple with 4 adverse lifestyle factors conceived compared to 52% with 3, 62% with 2, and 71% with one. Where no adverse lifestyle factors were present, 83% of couples became pregnant (Burton, 2014).

Delayed child bearing /age of starting a family

Human reproduction is greatly influenced by age. This is because so many physiological changes take place both in men and women as they grow older. This is also in addition to the powerful effect of socioeconomic and environmental factors which has not helped to improve reproductive potential despite improved technology and advancement in science (Bopp et al., 2008).

In men, semen parameters begin a steady decline as early as age 35 (Stone et al., 2013). Semen volume and motility decrease and morphology may become increasingly abnormal (Stewart, 2011). Although age affects both males and females, the most significant impact on reproduction is maternal age (Bretherick et al., 2010). A woman is born with all the egg cells she will ever have. They reduce in number and quality over the years and by the time she gets to 35 years, her fertility is declined (Baird et al., 2005). Incidence of genetic abnormality and spontaneous abortion also increases with maternal age (Kroon et al., 2011). A benchmark of natural fertility is usually provided by the Hutterite population which lives a relatively simple communal lifestyle that excludes the use of contraception. They showed a progressive decline in the rate of pregnancies with an

increase in female age (Tyden et al., 2006). The data of Wood demonstrates this with a 50% decrease in apparent fecundability at age 35 years. Fecundability is the ability to achieve a pregnancy within a menstrual cycle. This effect is also similar in women undergoing ART with decreased pregnancy rates with age (Liu et al., 2017). The biological clock regulating the female reproductive life span has existed to reduce the complications associated with abnormal pregnancy outcomes in advancing age and to save energy for somatic maintenance (Luo et al., 2011; Emokpae and Igharo, 2020). Despite this substantial evidence of a decline in fertility with age, men and women are often ignorant of the risk associated with delayed childbearing due to the increasing social behavior where education and career pursuits coupled with economic factors keep both genders out of relationships and childbearing until the late thirties and early forties (Varshini et al., 2012). Couples need to understand the biology of aging concerning fertility in both sexes to enable them and health-care givers to make an informed decision regarding delayed childbearing, age of starting a family, and counseling of those seeking fertility treatments (Emokpae and Igharo, 2020). Although men could produce semen even at an older age, increased paternal age has been reported to be a major determinant for testicular function (Bray et al., 2006; Janevic et al., 2014), sex hormones (Khera et al., 2016), sperm quality (Agarwal et al., 2008; Brahem et al., 2011), sperm DNA integrity (Moskortsev et al., 2006), telomere length (Brer et al., 2013), and epigenetic factors (Culey et al., 2011; Arslan et al., 2017). These changes due to aging adversely impact fecundity and reproductive outcomes such as congenital birth defects, fetal death, recurrent abortion, and infertility (Lian et al., 1986; Allo et al., 2012). Paternal age has also been linked with autism (D'Onofrio et al., 1995), Schizophrenia and bipolar disorders (Arslan et al., 2017), and achondroplasia (Orioli et al., 1995). Higher oxidative stress occurs in aged couples as a result of an imbalance between reactive oxygen species generation and available antioxidants in the circulation. This was aptly demonstrated in an experimental study that showed that aging leads to a decline in fertility and the numbers of Sertoli and germ cells in mice with the complete absence of Catalase (CAT-null(cat-/-) or/and Superoxide dismutase 1 (SOD-null(sod-/-)). This is an indication that these antioxidant enzymes are vital in the

maintenance of germ cell quality in advanced age. Paternal age is reported to adversely affect testicular volume (Johnson et al., 1988), alters the structure of seminiferous tubules (Janevic et al., 2014), and reduces blood supply to the testes. Sex hormone secretion is affected by aging; there is a decline in the secretion of testicular inhibin B by Sertoli cells coupled with increased secretion of follicle-stimulating hormone (FSH) (Ilacqua et al., 2018). Since there are reductions in the numbers of Leydig cells, the biosynthesis of testosterone is affected. Aging was also reported to alter the hypothalamic-pituitary-gonadal axis function, hence leading to changes in the other reproductive hormones (Wu et al., 2008). The exacerbated effect of aging on increased DNA fragmentation was reported to be a contributing factor to the low success rate of Assisted Reproduction Technology (ART) treatment in infertile couples (Carlini et al., 2017; Alvarez-Sedo et al., 2017). Therefore, spermatozoa of men with advanced age should be used with caution by infertility clinics to avoid the risk of possible genetic disorders in offspring.

Nutritional factors

Nutritional problems are strikingly different in developing nations where deprivation, under-nutrition, and malnutrition are the major problems while eating disorders and obesity are very common in developed countries. Obesity is however increasingly common in developing countries due to globalization. The reproductive system is extremely sensitive to influences from the external environment. This is because it involves energy expenditures and it is only sensible that the physiological control mechanisms of the reproductive axis be closely linked to the nutritional status as it is in living organisms (Giahi et al., 2016). Several factors such as genetic, environmental and behavior contribute to the increasing trend in overweight and obesity. Because of the preponderant of cheap high calorie but nutrient-poor foods in the last four decades, the prevalence of obesity has increased all over the world (Via, 2012).

In females, reproduction involves much greater energy expenditures than for males and as a protective mechanism against under-nutrition, ovarian activity is suppressed in women with eating disorders and exercise-induced amenorrhea through pathways in the

hindbrain. The combined prevalence of Bulimia nervosa and Anorexia nervosa is approximately 5% among women of reproductive age. Bulimia nervosa is an eating disorder that is characterized by binge eating which is followed by fasting or self-induced vomiting or purging. It is an emotional disorder that makes one have a distorted body image and an obsessive desire to lose weight. Anorexia on the other hand is also an eating disorder that is more of a psychological condition marked by extreme self-starvation due to a distorted body image. The likelihood of cure is higher with Bulimia nervosa. Both disorders suppress ovulation in severely affected women and account for up to 60% of women with anovulatory infertility (Tabler et al., 2018).

Some nutritional factors may affect male fertility and evidence suggesting a direct association between nutritional altitude and poor semen quality has emerged. High-fat diets inhibit reproduction by affecting the physical and molecular structure of not only sperm cells but also the developing fetus and offspring (Mitchell et al., 2011; Rato et al., 2014). Some experimental studies have shown that feeding mice with high-fat diets resulted in long-term alterations in the reproductive system, and the metabolic programming mechanisms; such as a decrease in both height and diameter of the seminiferous epithelium, and seminiferous tubules respectively (Erdemir et al., 2012; Ibanez et al., 2017). This also resulted in decreased sperm concentration, viability, and DNA integrity (Mortazari et al., 2014). It has long been recognized that normal testicular function is responsive to changes in whole-body metabolism, and that testicular metabolism can be affected by the intake of high-energy diet (Rato et al., 2013) and obesity. Studies have suggested that reproductive health can be enhanced by modification of dietary intakes such as fruits and vegetables (Mendiola et al., 2009; Braga et al., 2012), legumes (Braga et al., 2012), and fish (Attaman et al., 2012). The regular intake of diet rich in fruits, vegetables, legumes, and fish was associated with better sperm quality (Karayiannis et al., 2017) and a lower DNA fragmentation index than subjects who do not take such foods regularly. Regular intake of red meat was inversely associated with sperm quality (Afeiche et al., 2014). Table 1 shows the schematic representation of various lifestyle behaviors on infertility.

Table 1: Findings of lifestyle behaviors on infertility in Nigeria

First Author's name	Study Design	Population Size	Type of Lifestyle Behaviors	Reproductive Health Effect
Alabi OJ (2020)	Qualitative	15	Social, traditional and Religious beliefs	Low acceptance of surrogacy practice
Emokpae MA (2020)	Cross-sectional	400	Micronutrients	Poor semen quality
Emokpae MA (2020)	Cross-sectional	60	Petrol fumes	Low sex hormone levels
Ikyernum JA (2019)	Cross-sectional	600	Sexually transmitted infections	Poor semen quality
Emokpae MA (2019)	Experimental	24 rabbits	Drug abuse (Tramadol)	Increased lipid peroxidation
Osabuohien DO (2018)	Experimental	30 rabbits	Alcohol Abuse	Low sex hormone levels
Emokpae MA (2018)	Cross-sectional	122	Paternal aging	High oxidative stress and apoptosis
Adewumi (2017)	Review	Several articles	Cultural beliefs/Cost	High emotional/financial stress
Okafor NI (2017)	Cross-sectional survey	589	Perception and traditional belief	Unscientific perception, misconception of IVF treatment
Emokpae MA(2016)	Cross-sectional	60	Toxic metals	Poor semen quality
Emokpae MA (2015)	Cross-sectional	60	Toxic metals	Poor semen quality
Oremosu AA (2014)	Experimental	Sprague-Dawley Rats	Sex hormones, oxidative stress and semen quality	Low sex hormone levels, poor semen quality and high oxidative stress.
Omoaregba JO (2011)	Cross-sectional	100	Psychological stress	High Psychological distress
Makanjuola AB (2010)	Case-control	320	Psychological stress	High rate of psychiatric morbidity, lack of support from husbands and husbands' relatives.

Weight

Both obesity and low body weight are associated with alterations in the reproductive functions by causing hormone imbalance and ovulatory dysfunction. Abnormal weight is usually defined as a high body mass index (BMI) of ≥ 25 and a low BMI of < 18.5 (Brazier, 2018). In a study of health and lifestyle among Finnish men and women with infertility, it was reported that infertile women under 50 years consumed more unsaturated fat, less saturated fat, and consumed more alcohol than their fertile counterparts (Revonta et al., 2010). The effectiveness of lifestyle intervention was assessed among some obese infertile women, and the authors reported that lifestyle intervention increased the natural conception rate among anovulatory obese infertile subjects, but did not affect the rate of healthy live birth (van Oers et al., 2016). It is recognized that obesity does not only increase the risk of infertility but obese women are less likely to achieve conception after infertility treatment. The result of a multicenter randomized trial showed that lifestyle intervention led to a more spontaneous pregnancy among anovulatory infertile obese women compared to ovulatory women (van Oers et al., 2016). The study suggests that obese anovulatory women would benefit from a reduction in their weight during infertility treatment. Infertile women are therefore counseled to maintain a healthy weight as being overweight and underweight can impair ovulation naturally. The evaluation of lifestyle habits and the modification of unhealthy habits by trained health providers with specific management, like systematic folic acid supplementation in females attempting to conceive will yield the desired outcomes (Silvestris et al., 2019). High insulin levels and insulin resistance are associated with obesity, polycystic ovarian syndrome, metabolic syndrome, and all have serious implications for female infertility. Hyperinsulinaemia enhances the excess biosynthesis of androgen and lipids from the theca cells (Field et al., 2014). Obesity enhances the secretion of high leptin levels and leptin is a known stimulator of estrogen synthesis in the luteinized granulosa cells but also inhibits progesterone synthesis from insulin-stimulated theca cells. Some authors have used this mechanism to explain obesity-associated infertility (Silvestri et al., 2018). Increased

production of estrogen by the fat cells and primary sex organs that occur in obesity or a state of high body fat is interpreted as birth control by the body, hence limiting the chances of conception (Wasiu Eniola et al., 2012). In males, the plasma concentration of testosterone decreases as obesity increases due to reduced sex hormone-binding globulin (SHBG), but there seems to be a weight-related increase in estradiol and estrone levels in men (Chavarro et al., 2010). The quality and concentration of semen and motility of sperms were higher and the rate of sperm DNA damage was lower in men who had normal BMI when compared with obese men (Aydin et al., 2014). Some foods containing folate, antioxidants, and omega-3-fats are important for reproductive health (Aydin et al., 2014).

Smoking

Cigarette smoking has been associated with adverse effects on fertility although not widely recognized. It also increases the risk of congenital cardiac disease (Mateja et al., 2012). In males, smoking has been observed to reduce sperm concentration, morphology, and motility as well as increased DNA damage (Caserta et al., 2013). Tobacco smoke contains several substances such as nicotine, cadmium, lead, superoxide, and hydroxyl radicals that can adversely affect reproductive health. Superoxide and hydroxyl radicals can take part in the Fenton reactions to produce hydrogen peroxide and ultimately caused oxidative stress and cause DNA damage (Taha et al., 2012). Cadmium and lead have been reported to cause DNA strand breaks while nicotine, superoxide, and hydroxyl radicals can induce double-stranded DNA breaks in sperm DNA (Arabi, 2004). Smoking has been reported to cause a decrease in antioxidant levels in the body (Lesgards et al., 2002). A study that evaluated the levels of DNA fragmentation index (DFI) in infertile smokers and infertile non-smokers reported a significantly higher ($p < 0.001$) DFI (37.66%) among infertile smokers than infertile non-smokers (19.34%) and controls (14.51%) (Wright et al., 2014). The study demonstrated the contribution of smoking to infertility.

In females, there is an increased thickness of the zona pellucida in smokers which makes sperm penetration difficult (Shiloh et al., 2004).

Menopause has been reported to occur 1-4 years earlier in smoking women when compared to non-smoking women (Whitcomb et al., 2017). Cigarette contains several harmful constituents that have been detected in the follicular microenvironment of smokers such as cotinine and cadmium thereby altering hormone levels in the luteal phase and could affect the developing follicle (Dechanet et al., 2011). Smoking in women significantly decreases the chance of conception by disrupting ovarian function and depleting its reserve.

Oxidative stress is one of the main causes of DNA fragmentation in male infertility but may be modifiable in several ways. Sources of oxidative stress as outlined in this paper should be evaluated in infertile men as part of a treatment protocol. The use of antioxidants supplementation has been reported to have some benefits, but these antioxidant levels have to be determined whether there are deficiencies so that over-supplementation is avoided. It is important to maintain a delicate balance between oxidants/antioxidants to ensure fertility, successful fertilization, and pregnancy.

Alcohol consumption

Alcohol is the most commonly abused substance known and used for celebration and relaxation since ancient times (Rosenthal and Faris, 2017). Apart from damaging other organs of the body such as the liver, heart, and nervous system, it also affects reproductive health. The kind of damage done depends on the type, amount, and duration of alcohol consumption. Alcohol depletes many essential nutrients from the body such as vitamin B, zinc, iron, magnesium, calcium, sodium, potassium, etc; and these vitamins and minerals are needed for most functions including reproduction. There is excess estrogen and decrease testosterone in all types of alcohol abuse (Van Heertum and Rossi, 2017). Alcohol is a known teratogen and its consumption has been reported to decrease fertility (Dosumu et al., 2010). An animal study that evaluated the effect of chronic alcohol consumption on reproductive hormones and semen characteristics reported that serum testosterone, follicle-stimulating hormones (FSH), luteinizing hormone (LH), sperm count, and motility correlated inversely with increasing concentrations of alcohol consumed.

Concentration-dependent testicular morphological changes were also observed (Osabuohien and Emokpae, 2018). It was observed that chronic consumption of alcohol did not only lower the levels of sex hormones and sperm quality but also led to weight loss in the animals as a result of changes in dietary habits (Osabuohien and Emokpae, 2018). Chronic alcohol consumption also alters macronutrient and micronutrient absorption in the small intestine. Studies have shown that the absorption of amino acids, lipids, and glucose is impaired during chronic alcohol abuse (Sohrabvand et al., 2015). An earlier report indicated that chronic consumption of alcohol above 12% v/v concentration has the potential to increase serum markers of iron status and oxidative stress in experimental animals (Emokpae and Egho, 2017). It is suggested that chronic ingestion of high concentrations of alcohol may have adverse effects on sex hormones, testes, epididymis, and ultimately fertility potential. Therefore careful use of high concentrations of alcohol or better still abstinence is advised since alcohol suppresses the synthesis of hormones at the levels of the hypothalamus, the anterior pituitary, and the gonads ((Oremosu and Akang, 2014; Osabuohien and Emokpae, 2018). Damage to the nervous system in men can results in sexual impotence due to loss of libido and erection.

Alcohol is commonly consumed by women of reproductive age and is associated with several reproductive health risks. There is no data on the prevalence of alcohol use and abuse in Nigeria but 86.4% of people aged 18years and above are reported to have consumed alcohol at a point in their lives while 56% are current users in the United State of America (Abuse,2015). Studies in both human and animal models have observed that chronic alcohol consumption resulted in changes in ovulation and menstrual cycle regularity (Emmanuele et al., 2002; Schliep et al., 2015). Although acute alcohol consumption may not harm the menstrual cycle, it has been reported to negatively affect fertility treatment outcomes (Heertum and Rossi, 2017). Heavy alcohol drinking may lead to a decline in ovarian reserve and fertility potentials in women. Markers of ovarian reserve and fertility potentials (FSH, anti-mullerian hormone (AMH) and antral follicle count) were reported to be lower among alcohol users than non-users (Heertum and

Rossi, 2017). This was supported by evidence indicating that women who drink alcohol experience menopause at an earlier age than non-drinkers (Gavaler, 1985). On the contrary, there is no evidence linking mild or moderate alcohol consumption with female infertility. Some studies have reported no association between alcohol consumption and ovulation (Juhl et al., 2002) and fecundability (Parazzini et al., 1999; Mikklse et al., 2016). Even though the findings are inconsistent, individuals who are currently being treated for infertility are enjoined to abstain or reduce alcohol consumption.

A woman may suffer from infertility due to the derangement of the hormonal system by alcohol even with mild consumption. If she is pregnant there may be a risk of abortion and could also cause a low birth weight of the child with various congenital abnormalities if the pregnancy progresses (Mateja et al., 2012).

Those who start drinking early in life are more likely to indulge in unprotected sexual acts which can expose them to sexually transmitted diseases such as Chlamydia trachomatis and HIV/AIDS. Chronic dehydration is usually associated with heavy drinkers; appropriate hydration is important for a healthy reproductive function. Without enough water, men may experience poor quality erections, low seminal volume, and prostate infections. Women can develop persistent vaginal dryness and suffer greater susceptibility to a yeast infection (Richards, 2017).

Alcohol consumption and the effectiveness of IVF treatment

There is evidence that suggests that alcohol consumption negatively impacts ART treatment outcomes (Jensen et al., 1998). A prospective study of 221 subjects undergoing IVF or gamete intra-fallopian transfer (GIFT) reported a 13% decrease in the numbers of oocytes retrieved, a 2.86 times likelihood of not achieving pregnancy, and 2.21 times of higher risk of abortion among women who consume alcohol than controls (Klonoff-Cohen et al., 2003). These findings suggest fertilization failure, as alcohol intake can reduce the success rate of IVF treatment by decreasing oocyte yield and live birth rates. Therefore, women seeking IVF treatment are

encouraged to abstain or minimize alcohol consumption before commencing treatment.

Caffeine

Caffeine is a stimulant that has enabled it to be used as a beverage (tea, soft drink, chocolate, etc.). It affects the nervous system and various other organs including the reproductive system. It has over 1000 active compounds (stimulants), and a high intake of caffeine more than 5 cups or 500mg per day delays pregnancy. It interrupts egg fertilization and implantation process (Olsen, 2017). Several observational studies and meta-analyses have reported that maternal caffeine consumption may be associated with major adverse pregnancy outcomes. Some authors reported significant dose-dependent associations that are suggestive of causation while others observed no threshold of consumption below which associations were absent. Consequently, available data does not support health advice that assumes 'moderate' caffeine consumption during pregnancy is safe. However, current evidence supports pregnant women and would-be mothers to avoid caffeine consumption (James, 2020). Conversely, the American College of Obstetrics and Gynecologist (2010) implied that moderate caffeine did not harm the fetus of pregnant women but its high intake (more than 540 mg every day) resulted in low fetal weight and length. It also causes withdrawal symptoms such as headaches, nausea, irritability, etc. It may also increase the risk of miscarriage because it can cross the placenta barrier. A high level of caffeine consumption has been associated with an increased risk of stillbirth (Minguez-Alarcon et al., 2018). There is no definite amount or safe level of caffeine consumption but about 200mg is considered moderate for those breastfeeding, pregnant, or trying to conceive.

The regular consumption and abuse of high caffeine energy drinks are increasingly popular. These caffeine-rich energy drinks have been reported to readily pass through biological membranes and rapidly distributed all over the body and may impair male gonadal development and function (Bae et al., 2017). The mechanism by which caffeine impairs infertility is not well understood, and there are conflicting reports as

to its harmful effects by some authors (Ilacqua et al., 2018).

Physical exercise

Regular exercise affects all individuals' general health and wellbeing and probably provides some protection from obesity, cardiovascular disease, diabetes, psychological stress, etc. Exercise increases insulin sensitivity and improves ovarian functioning and may improve the chances of achieving conception. There is evidence to suggest an association between physical exercise and infertility, as exercise may contribute to a reduction in energy balance, leading to amenorrhoea and irregular ovulation (Redman, 2006). Physical exercise is beneficial to overweight or obese infertile women. The findings from an interventional study indicated that physical exercise combined with weight loss was associated with improved fertility among obese women (Clark et al., 1995). On the contrary, a cohort study of over 5000 women with a healthy BMI range (<25kg/m²) showed that rigorous exercise was inversely associated with fertility potentials, but was positively associated with fecundability among overweight and obese women (Wise et al., 2012). Sedentary lifestyle behavior refers to time spent doing little or no movement while awake or sitting. It is one important modifiable risk factor for infertility since biological evidence supports the association of physical activity and infertility. Women who engage in rigorous physical exercise may be at risk of infertility due to anovulation and implantation defect (Evenson and Hesketh, 2016).

Most researches about physical fitness and reproduction are primarily focused on athletes rather than those with moderate level fitness. After BMI adjustment, each hour of vigorous exercise per week was reported to be associated with a 5% reduction in risk to protect ovarian functioning. However, in obese infertile women, increased physical fitness, and psychological wellbeing resulted in significant improvement in ovulation and conception (Kort et al., 2014). Female athletes who engage in excessive exercise and have poor dietary habits are at risk of developing a low BMI which may result in a low estrogen level. This affects the menstrual cycle and ovulation (Evenson and Hesketh, 2016).

The quality of sperm parameters of men performing the exercise for one hour, at least three times a week were 15.2% better than that those who performed exercise less frequently or excessively (9.7%). The parameters investigated by the authors were the morphology, count, concentration, and motility (Aydin et al., 2014). There are however conflicting data on the effect of physical exercise on male fertility potential. Earlier studies have indicated that regular vigorous exercise can adversely affect semen quality and testicular function, a situation attributed to testicular heating (Hjollund et al., 2002), oxidative stress (Mastaloudis et al., 2001), DNA fragmentation, and gonadotropin inhibition (Safarinejad et al., 2009). Conversely, some authors have observed that individuals who engage in regular exercises had better semen quality than sedentary control subjects (Vaamonde et al., 2012; Lalinde-Acevedo et al., 2017). Others have reported that moderate regular training may reduce seminal plasma oxidative stress than rigorous regular exercise (Hajizadeh-Maleki et al., 2017). Regular moderate exercise is recommended and may improve fertility potential among infertile subjects since rigorous physical activities might expose individuals to an increased risk of poor reproductive function.

Psychological stress

This can be defined as any uncomfortable "emotional experience" accompanied by predictable biochemical, physiological, and behavioral changes or responses (Nargund, 2015). Many forms of stress including physical, social, or psychological is a modern lifestyle, which can affect reproduction. Stress may cause infertility or it may arise from infertility (Aydin et al., 2014) thereby affecting human reproduction. The autonomous nervous system and adrenal hormones take part in the classic stress response while also affecting the reproductive system (McGrady, 1984). The psychosocial-induced stress affects fertility via the limbic system which impairs gonadotrophin-releasing pulsation; leads to low serotonin secretion, elevated prolactin level, and ultimately to anovulation. Psychosocial stress can also cause abnormal function of the immune system which may adversely impact fertility-related antibodies (Brkovich and Fisher, 1998). It was reported that infertility is not solely a medical problem but also

causes psychosocial challenges such as anxiety, depression, violence, marital instability, and divorce (Makanjuola et al., 2010). Studies in Nigeria have revealed varying degrees of psychosocial challenges among infertile women. Procreation is considered as a means to enhance or solidify a woman's status in the family and community in Nigeria (Makanjuola et al., 2010). In a study of predictive factors for psychiatric morbidity among infertile women, it was observed that 48.8% out of 160 respondents presented with psychiatric morbidity. The absence of support from their husbands and husbands' relatives, unfair treatment, discrimination, and induced abortion were significantly higher ($p < 0.001$) among infertile women than control subjects. The psychosocial challenges were not different between primary and secondary infertile women. The authors emphasized early identification of psychiatric morbidity and more public enlightenment to enhance moral and psychosocial support for women with infertility in Nigeria (Makanjuola et al., 2010). Surprisingly, the reported rate of psychiatric morbidity (48.8%) was higher than previously reported from the same center (Abiodun et al., 1992). Some authors have reported a rate of 47.3% of psychiatric morbidity among infertile women from Akwa Ibom State in Nigeria. This is an indication that the challenge is widespread in Nigeria. Lack of support from their husbands, unfair treatment, and discrimination from their husbands and their relatives towards infertile women were associated with psychosocial problems (Abasiubong et al., 2008).

There is enough scientific evidence to suggest that psychological stress can severely affect spermatogenesis, mainly by depressing testosterone secretion. The hypothalamic-pituitary-adrenal (HPA) axis has a direct inhibitory action on the hypothalamic-pituitary-gonadal (HPG) axis and Leydig cells in the testes. The gonadotropin inhibitory hormone (GnIH) also has an inhibitory effect on the HPG axis which results in a fall in the testosterone levels, which causes changes in Sertoli cells and the blood-testis barrier leading to the arrest of spermatogenesis (Bhongade et al., 2014).

Stress activates an inhibitory effect on the female reproductive system. Corticotrophin releasing hormone (CRH) inhibits hypothalamic

gonadotropin-releasing hormone (GnRH) secretion, and glucocorticoids inhibit pituitary luteinizing hormone and ovarian estrogen and progesterone secretion. This effect is responsible for the "hypothalamic" amenorrhea of stress, which is observed in anxiety and depression, malnutrition, eating disorders, and chronic excessive exercise, and the hypogonadism of Cushing syndrome (Kalantaridou et al., 2004).

It is recommended that infertile couples are encouraged to undertake stress management programs such as periodic relaxing training to reduce psychological distress and improve conception rates (Silvestris et al., 2019).

Sexual behavior

Sexual promiscuity greatly increases the risk of sexually transmitted diseases like gonorrhea, chlamydia trachomatis, herpes, syphilis, and HIV. Many sexually active individuals are less likely to use contraceptives which may lead to sexually transmitted infections (STIs), and unintended pregnancies. The increased risk of unplanned pregnancy and criminal abortions further aggravates the risk of STIs and infertility. Sexually transmitted infections (STIs) are common problems often associated with infertility in Nigeria (Uadia and Emokpae, 2015). Studies have associated STIs with risk for male infertility in southern Nigeria (Okonofua et al., 2005), and men who reported having chronic penile discharge, painful micturition, genital ulcers, and testicular pain were more likely to be infertile. Another study reported 173/500 (34.6%) of STIs prevalence among males investigated for infertility in Kano, Northern Nigeria (Emokpae et al., 2009). Early diagnosis and treatment of STIs is key to the prevention of sexually transmitted infections-induced infertility.

Drug abuse

Women are more vulnerable to long term drug abuse compared to men due to the difference in physiology, weight, hormone levels, etc. that can affect the breakdown of these drugs in the body (Guarnotta, 2016). Heroin and methadone are known to cause amenorrhea. Intravenous drug use exposes one to HIV and AIDS. When someone is under the influence of such drugs that individual can partake in risky sexual acts

that make him or her susceptible to sexually transmitted infections (STI), including Human Papilloma Virus (HPV). This is linked to increased cervical cancer risk among women. Drugs such as marijuana, heroin, methamphetamine and cocaine could easily pass through the placenta to the fetus thereby increasing the risk of low birth weight, birth defects, premature birth, sudden infant death syndrome (SIDS), and changes in physical features of the fetus. Women who use illicit drugs during pregnancy are up to two times more likely to have a stillbirth, as prescription drugs such as non-steroidal anti-inflammatory drugs NSAID show a correlation with female infertility (Forray., 2016).

In males, this risky behavior produces similar outcomes of STIs and infertility which usually presents with problems of sexual dysfunction. The use of methamphetamine and cocaine can lead to erectile dysfunction and delayed orgasm in men who initially may have experienced benefits such as heightened arousal. Chronic use of marijuana decreases testosterone secretion from Leydig cells, spermatogenesis, sperm motility, etc. (Fronczak et al., 2012). Marijuana contains "hashish" which also is capable of binding to receptors in a reproductive organ such as the uterus and ductus deference (Aydin et al., 2014).

Occupational risk factors and toxic metals

The environment in which one works and carries out daily activities may increase the risk of exposure to various chemicals that have potentially negative effects on reproductive health. Some results suggest deterioration of reproductive health indices in many industrialized countries in recent times (Kumar et al., 2018).

In addition to the adverse effects of toxic metals exposure with the industrial products, residues of insecticides were encountered in higher quantities in the urine of men engaged in gardening as a hobby, agriculture and greenhouse work; and this decreased semen quality. These toxic metals include lead, mercury, boron, arsenic, cadmium, etc. Cadmium and lead have been reported to adversely affect semen quality among infertile men (Emokpae and Adobor, 2016). Recent data

indicate that serum levels of FSH, LH, estradiol, progesterone, and testosterone were significantly lower among fuel attendants than non-occupationally exposed control subjects.

Mean levels of blood cadmium and lead were significantly higher among fuel attendants than controls. The measured sex hormone levels, FSH ($r=-0.50$, $p=0.001$), LH ($r=-0.52$, $p=0.001$), estradiol ($r=0.32$, $p=0.009$), progesterone ($r=-0.35$, $p=0.005$) and testosterone ($r=-0.48$, $p=0.001$) correlated with the duration of exposure to petrol fumes. Exposure to petroleum fumes may be a risk factor and may be associated with reproductive hormone abnormalities. Personal protective devices should be worn by petrol attendants to avoid the adverse consequences of exposure (Emokpae and Oyakhire, 2020).

Cellular phones and radiation

Emerging evidence suggests the detrimental effect of cellular phones on fertility. The numbers of mobile phone users are increasing by the day and several users keep and/or store mobile phones in their trouser pockets. The mobile phone has been suggested as a source of damaging radiation to the male reproductive organs. Increased levels of DNA fragmentation index have been reported in mobile phone users (Wright et al., 2014). These gadgets transmit or receive radiofrequency electromagnetic waves that have adverse effects on sperm motility, number, and morphology. Higher serum free testosterone and a lower luteinizing hormone (LH) level were reported among some users of cellular phones than control subjects who do not use cellular phones (Gutschi et al., 2011).

Religious belief

Another major challenge is the wrong perceptions and religious beliefs among the non-enlightened majority in developing countries particularly in West Africa where people believe that babies born through Assisted Reproductive Techniques (ART) are not "real babies". This belief is very common among the uneducated and so strong that even the educated have some reservations due to the strong family support system being practiced. As a result, there is usually a delay in the willingness to access treatment because they want to "wait on

God" for the natural process of conception. This practice further reduces the chances of hitherto healthy individuals that would have benefited from the treatment particularly those with unexplained infertility who could afford the cost of the technique. Therefore, individuals have a responsibility to preserve or increase their fertility potential to some degree by modifying their lifestyle behaviors which may improve or hamper their reproductive health. The perception of women in a study conducted in the South-eastern state of Nigeria regarding infertility and IVF treatment is that of superstition, misconception, and poor awareness. The respondents perceived infertility as supernatural and destiny based, and IVF treatment as unnatural and expensive. The authors advocated reproductive health education to create the necessary awareness of the etiologies of infertility and the importance of IVF treatment as a means of conceiving 'natural' babies.

Some factors impairing effective treatment of infertility.

Some of the identified factors militating against the effective treatment of infertility include; high cost and inaccessibility of most couples in need, absence of specific objectives, priorities, and strategies for infertility care in most countries in sub-Saharan Africa, absence of reliable data and good follow up mechanisms, lack of integration of infertility services into the reproductive health services, absence of proper coordination of the health care system, inability to accurately target those at risk for infertility and inadequate training and research in infertility (Leke, 2019). Some authors in Nigeria have observed that despite the great burden of the condition, only very few infertility management programs are available (Omoaregba et al., 2011). Fertility care, development, and access are limited. Therefore, the burden of infertility lies solely on the couple (Mohammed-Durosini, 2019). It was observed that most infertile couples belong to the very poor in the society, hence would not be able to afford the high cost of treatment (Agholor, 2017). As a result, most couples discontinue or abandon their treatment. The most common cause of female infertility in Nigeria is a pelvic factor especially tubal blockage (probably due to post-infectious causes such as sexually transmitted

infections, post abortal, and puerperal sepsis) and the best treatment is by Assisted Reproductive Technology methods. The cost of a cycle of In-vitro Fertilization is above one million Naira. To make matter worse, the success rate is low (20-30%), and as such a couple may require more than one cycle to achieve success. This does not only lead to emotional and psychological trauma but increase poverty. (Agholor, 2017).

Practical recommendations to modify lifestyle behaviors

Age plays a major role in determining the fertility of both partners. Couples need to consider the age of the partners before marriage so that the chances of conception are increased. The peak of fecundability is before age 35 for men and 30 for women. Infertile couples should access care early after a maximum of one year without conception and six months among older couples.

Couples trying to achieve pregnancy should limit or quit smoking since there appears to be a significant impact of smoking on reproductive outcomes. The risk of miscarriage will be reduced and menopause will be delayed by 4 years. Passive smoking should be avoided.

Research shows that weight plays a significant role in fertility. Therefore; maintaining an ideal weight will help to prevent hormonal imbalance which adversely affects fertility thereby improving ovulation and the risk of miscarriage and other complications. Over-weight infertile women on treatment are encouraged to reduce weight for effective treatment outcomes.

It is better to reduce or abstain from alcohol consumption when trying to achieve pregnancy. Caffeine also appears to have a negative effect and should also be consumed with caution.

Infertile couples should avoid anxiety and emotional stress, but embark on relaxation programs to reduce other sources of stress to increase fertility. Moderate regular exercises could help to release endorphins which would help relaxation.

Nutrition and exercise may impact fertility both in men and women. Good nourishment and a

balanced diet should be encouraged. Infertile women should consume foods low in saturated fat and red meat, and high in vegetables, legumes, and antioxidants.

Recreational and prescription drugs have a significant impact on fertility as most of these drugs alter reproductive processes. It is therefore best to avoid all unnecessary medications and recreational drugs.

Environmental/occupational exposures can be minimized by wearing personal protective equipment (PPE). Adequate monitoring and adherence to the protocol by regulatory authorities is advocated. Excessive irradiation can be avoided by reducing contact with electronic gadgets like mobile phones that emit electromagnetic waves. It is not possible to eliminate all hazards in the environment, but efforts can be made to reduce them.

Conclusion

Most lifestyle factors are theoretically modifiable habits which can be reversed with strong determination by affected subjects. Public enlightenment by health care providers will go a long way to increasing the knowledge and improve the awareness of the population since most are not aware of the potential consequences of lifestyle habits on infertility. Counseling of infertile couples may enhance awareness of the risk of lifestyle behaviors and facilitate appropriate lifestyle change that might improve reproductive health. Educational and career pursuit could be combined with childbearing and the government should provide facilities such as day-care and nursery within the working environment to encourage prospective mothers. Public health enlightenment campaigns that will educate on the harmful effects of drug and substance abuse should be intensified. Appropriate legislation and enforcement of laws that regulate these drugs coupled with the punishment of offenders may help to check the negative impact of substance abuse by individuals and society at large.

References

Abasiubong F, Bassey E, Ekett J, Umoiyoho A, Umoh A (2008). The burden of psychological symptoms in gynaecological conditions among

women in Uyo, Akwa Ibom, Nigeria. *Niger J Psychiat*, 6: 21-25.

Abiodun AO, Adetoro OO, Ogunbode O.O (1992). Psychiatric Morbidity in a gynaecology Clinic in Nigeria. *J Psychosomatic Res*, 36: 488-490.

Abuse S, Mental Health Services Administration (SAMHSA). National Survey on Drug Use and Health (NSDUH). 2015:2016.

Adewumi EA(2017). Infertility treatment Financing in Nigeria. *Niger J Health Scis*, 17(1):38-42.

Afeiche MC, Williams PL, Gaskins AJ, Mendiola J, Jørgensen N, Swan SH, et al (2014). Meat intake and reproductive parameters among young men. *Epidemiology*. 2014;25:323–330.

Agarwal A, Makker K, Sharma R (2008). Clinical relevance of oxidative stress in male factor infertility: an update. *Am J Reprod Immunol*. 59:2–11.

Agholor K(2017). The burden of infertility in Nigeria: Raising Visibility to Promote Equitable Access to Care. Maternal Health TaskForce at the Harvard Chan School, Center of Excellence in Maternal and Child Health. www.mht.org. accessed 08/09/2020.

Alabi OJ(2020). A Qualitative investigation of Surrogacy as a panacea for infertility in Nigeria. *F1000 Res*, 9:103.

Alio AP, Salihu HM, McIntosh C, August EM, Weldelesasse H, Sanchez E, et al (2012). The effect of paternal age on fetal birth outcomes. *Am J Mens Health*.6:427–435.

Alvarez Sedó C, Bilinski M, Lorenzi D, Uriondo H, Noblía F, Longobucco V, et al (2017). Effect of sperm DNA fragmentation on embryo development: clinical and biological aspects. *JBRA Assist Reprod*. 2017;21:343–350.

American College of Obstetrics and Gynecologists (2010). Moderate Caffeine Consumption During Pregnancy by the Committee on Obstetrics Practice, number 462.

Anderson K, Nisenblat V, Norman R (2010). Lifestyle factors in people seeking infertility treatment - a review. *Austr N Zeal J Obstetr Gynaecol*,50:8–20.

Arabi, M., 2004. Nicotinic infertility: assessing DNA and plasma membrane integrity of human spermatozoa. *Andrologia* 36,305–310.

Araoye MO (2003). Epidemiology of Infertility: Social Problems of the infertile couples. *West Afr J Med* 22(2):190-196.

Arslan RC, Willführ KP, Frans EM, KJH V, Bürkner PC, Myrskylä M, et al (2017). Older fathers' children have lower evolutionary fitness across four centuries and in four populations. *Proc Biol Sci.*379:385..

Attaman JA, Toth TL, Furtado J, Campos H, Hauser R, Chavarro JE (2012). Dietary fat and semen quality among men attending a fertility clinic. *Hum Reprod.*27:1466–1474.

Aydin, T., Karadag, M., Demir, A., Cecen, K., Karasu, Y. Ulker, K (2014). Effect of modification of lifestyle on reproductive potential. *Kafka's J Med Scis*; 4(1):27-35.

Bae J, Choi H, Choi Y, Roh J. Dose- and time-related effects of caffeine on the testis in immature male rats. *Exp Anim.* 2017;66(1):29–39.

Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C (2005). Being Big and Growing Fast: Systematic review of size and growth in infancy and later obesity. *BMJ* 331:929.

Bhonage, M B., Prasas S., Jiloha, R C., Ray, PC., Mohapatra, S., Knowler, B C (2014). Effect of psychological stress on fertility hormone and seminal quality in male partners of infertile couples. *Andrologia* 47; 336-342.

Bopp, B.L., Seifer, D.B., (2008). Age and reproduction. *Glob Lib Women's Med.* ISSN: 1756-2228 [DOI:10.3843/GLOWM.10341]

Braga D, Halpern G, Figueira R, Setti AS, Iaconelli A Jr, Borges E Jr (2012). Food intake and social habits in male patients and its relationship to intracytoplasmic sperm injection. *Fertil Steril.*97:53–59.

Brahem S, Mehdi M, Elghezal H, Saad A (2011). The effects of male aging on semen quality, sperm DNA fragmentation and chromosomal abnormalities in an infertile population. *J Assist Reprod Genet.* 28:425–32.

Bray I, Gunnell D, Davey SG (2006). Advanced paternal age: how old is too old? *J Epidemiol Commun Health.* 60:851–853.

Bretherick KL, Fairbrother N, Avila L, Harbord SHA, Robinson WP (2010). Fertility and aging: do reproductive-aged Canadian women know what they need to know? *Fertil Steril* 93(7):2162–2168.

Brkovich AM, Fisher WA (1998). Psychological distress and infertility: forty years of research. *J Psychosomatic Obstet Gynaecol*, 19: 218-228.

Broer L, Codd V, Nyholt DR, Deelen J, Mangino M, Willemsen G, et al (2013). Meta-analysis of telomere length in 19,713 subjects

reveals high heritability, stronger maternal inheritance and paternal age effect. *Eur J Hum Genet.*21:1163–1168.

Burton, P (2014). Lifestyle Factors and Fertility. Concept Fertility center, Version 5:1-3. www.conceptfertility.com.au. Accessed 18/09/2019.

Carlini T, Paoli D, Pelloni M, Faja F, Dal Lago A, Lombardo F, et al (2017). Sperm DNA fragmentation in Italian couples with recurrent pregnancy loss. *Reprod BioMed Online.* 2017;34:58–65.

Caserta, D., Bordi, G., Di segni, N., D'ambrosio, A., Mallozzi, M., Moscarini, M (2013). The influence of cigarette smoking on a population of infertile men and women. *Arch Gynecol Obstet.* 287:813-818.

Clark AM, Ledger W, Galletly C, Tomlinson L, Blaney F, Wang X, Norman RJ (1995). Weight loss results in significant improvement in pregnancy and ovulation rates in anovulatory obese women. *Hum Reprod*, 10:2705-2712.

Curley JP, Mashoodh R, Champagne FA (2011). Epigenetics and the origins of paternal effects. *Horm Behav.*59:306–314.

D'Onofrio BM, Rickert ME, Frans E, Kuja-Halkola R, Almqvist C, Sjolander A, et al (2014). Paternal age at childbearing and offspring psychiatric and academic morbidity. *JAMA Psychiatry.*71:432–438.

Damayanathi Durairajanayagam (2018) Lifestyle causes of male infertility, *Arab J Urol*, 16;1: 10-20.

Dosumu OO, Akinola OB, Akang EN (2010). Alcohol-induced testicular oxidative stress and cholesterol homeostasis in rats- the therapeutic potential of virgin coconut oil. *Middle East Fertil Soc J*,17:122-128.

Emanuele MA, Wezeman F, Emanuele NV (2002). Alcohol's effects on female reproductive function. *Alcohol Res Heal.* 26:274–281.

Emokpae M.A, Ogunniyi O.B, Dada G.O , Awopetu V.I (2019). Alteration in the levels of some markers of Oxidative Stress and liver function induced by Tramadol Administration in Male Rabbits: the effect of its withdrawal. *J Med Discov*, 4(1):1-4.

Emokpae MA, and Moronkeji MA (2020). Association of Copper-to Zinc Ratio with Sperm Concentration among Males Investigated for Infertility. *J Infertil Reprod Biol*, 8(3):49-52.

Emokpae MA, Igharo OG (2020). Linking Senescence, apoptosis and Oxidative stress in fertility. In: VR Preedy and VB Patel ed. *Aging:*

Oxidative Stress and Dietary Antioxidants, 2nd Ed., Academic Press, ELSEVIER London, UK, p. 113-123.

Emokpae MA, Oyakhire FO (2020). Levels of some reproductive hormones, cadmium and lead among fuel pump attendants in Benin City, Nigeria. *Afr J Med Health Scis*, 19(6), 70-77.

Emokpae, M.A and Chima, H. (2018). Effect of senescence on some apoptosis and oxidative stress markers in infertile normozoospermic and oligozoospermic men: A cross-sectional study. *Int J Reprod BioMed* 16(7): 435-442.

Emokpae, M.A and Egho, J.A. (2017). Chronic exposure to high alcohol concentrations in experimental animals may induce Iron overload and Oxidative stress. *Biokemistri* 29(1):24-30.

Emokpae, M.A, Adobor, C, Ibadin, K. (2016). Seminal Plasma levels of lead and mercury in infertile males in Benin City, Nigeria. *Int J Med Res Health Scis*,5(1):1-6.

Emokpae, M.A, Adobor, C.A. (2015). Association of seminal plasma cadmium levels with semen quality in non-occupationally exposed infertile Nigerian males. *J Environment Occup Scis*, 3(4):40-43.

Emokpae, M.A, Uadia PO, Nasir, S.M. (2009). Contribution of bacterial infection to Male infertility in Nigerians. *Online J Health Allied Scis*,8(1):1-6.

Emokpae, M.A, Uadia PO, Nasir, S.M. (2009). Contribution of bacterial infection to Male infertility in Nigerians. *Online J Health Allied Scis*,8(1):1-6.

Erdemir F, Atilgan DMF, Boztepe O, Siha-àrlaktas B, Sahin S (2012). The effect of diet induced obesity on testicular tissue and serum oxidative stress parameters. *Actas Urológicas Españolas*. 36:153–159.

Evenson KR, Hesketh KR (2016). Studying the Complex Relationship between Physical Activity and Infertility. *Am J Lifestyle Med*, 10(4):232-234.

Fehintola AO, Fehintola FO, Ogunlaja OA, Awotunde TO, Ogunlaja IP, Onwudiegwu U(2017). Social meaning and consequences of infertility in Ogbomoso, Nigeria. *Sudan J Med Sci*,12(2):9

Field SL, Dasgupta T, Cummings M, Orsi NM (2014). Cytokines in ovarian folliculogenesis, oocyte maturation and luteinisation. *Mol Reproduc Dev*. 81:284–314.

Forray A(2016). Substance Use During Pregnancy. *F1000 Res*, 5:F1000 Faculty Rev-887.

Fronczak, C.M., Kim, E.D., Barqawi, A.B., (2012). The insult of illicit drugs use on male fertility. *J Androl*, 33:515-528.

Gavaler JS (1985). Effects of alcohol on endocrine function in postmenopausal women: a review. *J Stud Alcohol*. 46:495–516.

Giahi L, Mohammadmoradi S, Javidan A, Sadeghi MR(2016). Nutritional Modifications in male infertility: a systematic review covering 2 decades. *Nutr Rev* 74(2):118-130.

Guarnotta, E. (2016). Effects of drug abuse on male and female reproductive systems. www.drugabuse.com. Accessed on 10/10/2019.

Gutsch, T., Mohammad A.B, Shamloul, R., Pummer, K., Trummer, H., (2011). Impact of cell phone use on men's semen parameters. *Andrologia*; 43(5):312-316.

Hajizadeh Maleki B, Tartibian B, Chehrazi M (2017). The effects of three different exercise modalities on markers of male reproduction in healthy subjects: a randomized controlled trial. *Reproduction*. 153:157–174.

Handelsman DJ, Staraj S (1985). Testicular size: the effects of aging, malnutrition, and illness. *J Androl*, 6:144–151.

Hjollund NH, Storgaard L, Ernst E, Bonde JP, Olsen J (2002). The relation between daily activities and scrotal temperature. *Reprod Toxicol*. 16:209.

Homan, G.F., Davies, M., Norman R., (2007). The impact of lifestyle factors on reproductive performance in general population and those undergoing infertility treatment: a review. *Hum Reprod update*; 13(3):209-223.

Ibáñez CA, Erthal RP, Ogo FM, MNC P, Vieira HR, Conejo C, et al (2017). A High Fat Diet during Adolescence in Male Rats Negatively Programs Reproductive and Metabolic Function Which Is Partially Ameliorated by Exercise. *Front Physiol*. 8:807.

Ikyernum JA, Agbecha A, Hwande ST(2019). Semen Profile of men presenting with infertility at First Fertility Hospital, Makurdi, North-Central Nigeria. *Clin Med Diagn*,9(2):26-35.

Ilacqua A, Francomano D, Aversa A (2018). The physiology of the testis. In: Belfiore A, LeRoith D, Eds. *Principles of Endocrinology and Hormone Action*, Endocrinology. Switzerland: Springer International Publishing AG; p.1–38.

Ilacqua A, Izzo G, Emerenziani GP, Balari C, Aversa A (2018). Lifestyle and Fertility: the

Influence of Stress and Quality of life on Male Fertility. *Reprod Biol Endocrinol*, 16:115.

James JE (2020). Maternal caffeine consumption and pregnancy outcomes: a narrative review with implications for advice to mothers and mothers-to-be. *BMJ, Evidence Based Med*, 111432.

Jensen TK, Hjollund HI, Henriksen TB, Scheike T, Kolstad H, Giwercman A, et al (1998). Does moderate alcohol consumption affect fertility? Follow up study among couples planning first pregnancy. *BMJ*. 317.

Johnson L, Abdo JG, Petty CS, Neaves WB (1988). Effect of age on the composition of seminiferous tubular boundary tissue and on the volume of each component in humans. *Fertil Steril*. 1988;49:1045–1051.

Juhl M, Andersen A-MN, Grønbaek M, Olsen J (2002). Moderate alcohol consumption and waiting time to pregnancy. *Hum Reprod*. 16:2705–2709.

Kalantaridou, S.N, Makrigianakis, A., Zoumakis, E., Chrousos, G.P. (2004). Stress and the Female Reproductive System. *J Reprod Immunol*, 62(1-2)61-68.

Karayiannis D, Kontogianni MD, Mendorou C, Douka L, Mastrominas M, Yiannakouris N (2017). Association between adherence to the Mediterranean diet and semen quality parameters in male partners of couples attempting fertility. *Hum Reprod*. 32:215–222.

Khera M, Broderick GA, Carson CC 3rd, Dobs AS, Faraday MM, Goldstein I, et al (2016). Adult-Onset Hypogonadism. *Mayo Clin Proc*. 91:908–926.

Klonoff-Cohen H, Lam-Kruglick P, Gonzalez C (2003). Effects of maternal and paternal alcohol consumption on the success rates of in vitro fertilization and gamete intrafallopian transfer. *Fertil Steril*. 79:330–339.

Kort, D., Winget, C., Kim, S.H, Lathi, R.B. (2014). A retrospective cohort study to evaluate the impact of meaningful weight loss on fertility outcomes in an overweight population with infertility. *Fertil Steril* 101(5):1400-1403.

Kroon, B., Harrison, K., Martin, N., Wong, B., Yarsdani, A., (2011). Miscarriage Karyotype and its relationship with maternal body mass index, age, and mode of conception. *Fertil Steril* 95(5):1827-1829.

Kumar, S., Thaker, R., Verma, V., Gor, M., Agarwal, R., Mishra, V., (2018). Occupational, environmental exposure and lifestyle factors:

Declining male reproductive health. *J Gynecol Infertil*. 1(1):1-5.

Lalinde-Acevedo PC, BJM M-T, Agarwal A, du Plessis SS, Ahmad G, Cadavid AP, et al (2017). Physically Active Men Show Better Semen Parameters than Their Sedentary Counterparts. *Int J Fertil Steril*. 11:156–165.

Leke RJI (2019). The prevalence of infertility and its preventive measures in sub-Saharan Africa. Presentation at the WHO-AFRO and EMRO Regional management of infertility workshop. www.gfmer.ch/medical_education. Accessed 08/09/2020.

Lesgards, J.F., Durand, P., Lassarre, M., Stocker, P., Lesgards, G., Lanteaume, A., Prost, M., Lehucher-Michel, M.P., 2002. Assessment of lifestyle effects on the overall antioxidant capacity of healthy subjects. *Environ. Health Perspect*. 110, 479–486.

Lian ZH, Zack MM, Erickson JD (1986). Paternal age and the occurrence of birth defects. *Am J Hum Genet*. 39:648–660.

Liu, K.E, Case, A., Cheung, A.P., (2017). Advanced reproductive age and fertility: No 346, *Int J Obstet Gynecol*. 39 (8):685-695.

Luo S, Murphy CT (2011). *Caenorhabditis elegans* reproductive aging: regulation and underlying mechanisms. *Genesis*, 49(2):53–65.

Makanjuola AB, Elegbede AO, Abiodun OA (2010). Predictive factors for Psychiatric morbidity and Women with infertility attending a gynaecology clinic in Nigeria. *Afr J Psychiat* 13:36-42.

Mastaloudis A, Leonard SW, Traber MG (2001). Oxidative stress in athletes during extreme endurance exercise. *Free. Radical Biol Med*. 31:911–922.

Mateja, W.A., Nelson, D.B., Kroelinger, C.D., Ruzek, S., Segal, J., (2012). Association between maternal alcohol use and smoking in early pregnancy and congenital cardiac defects. *J women's health*; 21(1):26-34.

McGrady A., (1984). Effect of psychological stress on male reproduction: A review. *Arch Androl*. 13 (1):1-7.

Mendiola J, Torres-Cantero AM, Moreno-Grau JM, Ten J, Roca M, Moreno-Grau S, et al (2009). Food intake and its relationship with semen quality: a case-control study. *Fertil Steril*. 91:812–818.

Mikkelsen EM, Riis AH, Wise LA, Hatch EE, Rothman KJ, Cueto HT, et al (2016). Alcohol consumption and Fecundability: a prospective Danish cohort study. *BMJ*. 31;354:i4262.

- Minguez-Alarcon, L., Chavarro, J., Gaskins, A., (2018). Caffeine, alcohol, smoking and reproductive outcomes among couples undergoing assisted reproductive technology treatment. *Fertil Steril*, 110(4):587-592
- Mitchell M, Bakos HW, Lane M (2011). Paternal diet-induced obesity impairs embryo development and implantation in the mouse. *Fertil Steril*.95:1349–1353.
- Mohammed-Durosinlorun A, Adze J, Bature S, Abubakar A, Mohammed C, Taingson M, Airede L(2019). Use and Pattern of previous care received by infertile Nigerian women. *Fertil Res Pract*, 5:14.
- Mortazavi M, Salehi I, Alizadeh Z, Vahabian M, Roushandeh AM (2014). Protective effects of antioxidants on sperm parameters and seminiferous tubules epithelium in high fat-fed rats. *J Reprod Infertil*.15:22–28.
- Moskovtsev SI, Willis J, Mullen JB (2006). Age-related decline in sperm deoxyribonucleic acid integrity in patients evaluated for male infertility. *Fertil Steril*. 85:496–499.
- Nargund, V.H (2015). Effects of psychological stress on male fertility. *National Rev Urol*, 12(17):373-382.
- Okafor NI, Joe-Ikechebelu NN, Ikechebelu JJ(2017). Perceptions of Infertility and In-vitro Fertilization Treatment among Married couples in Anambra State, Nigeria. *Afr J Reprod Health*, 2017;21:55-66.
- Okonofua F, Menakaya U, Onemu SO, Omo-Aghoja LO, Bergstrom S.A (2005). Case-Control Study of Risk Factors for Male infertility in Nigeria. *Asian J Androl* 2005;7:351-361.
- Olsen, N., (2017).Effect of caffeine on your body. Health line newsletter, www.healthline.com. Accessed 10/09/2019.
- Ombet W, Cooke I, Dyer S, Serour G, Devroey P (2008). Infertility and the provision of infertility medical services in developing countries. *Hum Reproduc Update*. 14:605–621.
- Omoaregba JO, James BO, Lawani AO, Morakinyo O, Olotu OS (2011). Psychosocial characteristics of female infertility in a tertiary health institution in Nigeria. *Ann Afr Med*, 10(1):19-24.
- Oremosu AA, Akang EN(2014). Impact of Alcohol on male reproductive hormones, oxidative stress and semen parameters in Sprague-Dawley rats. *Middle East Fertil Soc J*, 20:114-118.
- Orioli IM, Castilla EE, Scarano G, Mastroiacovo P (1995). Effect of paternal age in achondroplasia, thanatophoric dysplasia, and osteogenesis imperfecta. *Am J Med Genet*. 59:209–217.
- Osabuohien D.O, Emokpae M.A(2018). The Impact of Chronic Alcohol Consumption on Sex Hormones and Semen parameters in Male Rabbits. *The Niger Health J*, 18(4):148-156.
- Parazzini F, Chatenoud L, Di Cintio E, La Vecchia C, Benzi G, Fedele L (1999). Alcohol consumption is not related to fertility in Italian women. *BMJ*.;318:397.
- Rato L, Alves MG, Cavaco JE, Oliveira PF(2014). High-energy diets: a threat for male fertility? *Obes Rev*. 15:996–1007.
- Rato L, Alves MG, Dias TR, Lopes G, Cavaco JE, Socorro S, et al (2013). High-energy diets may induce a pre-diabetic state altering testicular glycolytic metabolic profile and male reproductive parameters. *Andrology*.1:495–504.
- Redman LM (2006). Physical activity and its effects on reproduction. *Reprod Biomed Online*. 12:579-586.
- Revonta M, Raitanen J, Sihvo S, Koponen P, Klemetti R, Männistö S, Luoto R (2010). Health and life style among infertile men and women. *Sex Reprod Healthcare*, 1(3):91-98.
- Richard, L., (2017) Reasons why Alcohol is bad idea while fighting candida. *Candida Diet Magazine*. www.thecandidadiet.com. Accessed 12/10/2019.
- Rosenthal RJ, Faris SB (2017). The Etymology and Early History of Addiction. *Addiction Res Theory*, 27(5):1
- Safarinejad MR, Azma K, Kolahi AA (2009). The effects of intensive, long-term treadmill running on reproductive hormones, hypothalamus-pituitary-testis axis, and semen quality: a randomized controlled study. *J Endocrinol*.200:259–271.
- Santos M, Rodriguez-Gonzalez GL, Ibanez C, Vega CC, Nathanielsz PW, Zambrano E (2015). Adult exercise effects on oxidative stress and reproductive programming in male offspring of obese rats. *Am J Physiol Regul Integr Comp Physiol*, 308: R219–R225.
- Sasano N, Ichijo S (1969). Vascular patterns of the human testis with special reference to its senile changes. *Tohoku J Exp Med*. 99:269–280.
- Schliep KC, Zarek SM, Schisterman EF, Wactawski-Wende J, Trevisan M, Sjaarda LA, et al. (2015).Alcohol intake, reproductive

hormones, and menstrual cycle function: a prospective cohort study. *Am J Clin Nutr.* 102:933–942.

Selvaratnam JS, Robaire B (2016). Effects of Aging and Oxidative Stress on Spermatozoa of Superoxide-Dismutase 1- and Catalase-Null Mice. *Biol Reprod*, 95(3):60,1-13.

Sharma, R., Biedenharn, K.R., Fedor, J.M., Agarwal, A., (2013). Lifestyle factors and Reproductive Health: Taking control of your fertility. *Reproductive biology endocrinology* 11:66.

Shiloh H, Lahav-Baratz S, Koifman M, Ishai D, Bidder D, Weiner-Meganz Z, Dirnfeld M (2004) The impact of cigarette smoking on zona pellucida thickness of oocytes and embryos prior to transfer into the uterine cavity. *Hum Reprod* 19, 157-159.

Silvestris E, de Pergola G, Rosania R, Loverro G (2018). Obesity as disruptor of the female fertility. *Reproduc Biol Endocrinol.* 16:22.

Silvestris E, Lovero D, Palmirotta R (2019). Nutrition and Female Fertility: an Independent Correlation. *Frontiers Endocrinol* 10:346.

Sohrabvand F, Jafari M, Shariat M, Haghollahi F, Lotfi M(2015). Frequency and Epidemiologic Aspects of Male infertility. *Acta Med Iran*, 53:231-235.

Stewart, A.F. and Kim, E.D., (2011). Fertility concerns for the ageing male. *Urology Journal*, 78(3):496-499.

Stone, B.A., Alex, A., Werlin, L.B., Marrs, R.P., (2013). Age threshold for changes in Semen parameters in men. *Fertil Steril*, 100:952-958.

Tabler, J., Utz, R.L., Smith, K.R., Hanson, H.A., Geist, C (2018). Variations in reproductive outcomes of women with histories of bulimia nervosa, anorexia nervosa or eating disorder not otherwise specified relative to the general population and closest aged sister. *Int J Eat Disorder*, 51(2):102-111.

Taha, E.A., Ez-Aldin, A.M., Sayed, S.K., Ghandour, N.M., Mostafa, T., 2012. Effect of smoking on sperm vitality, DNA integrity, seminal oxidative stress, zinc in fertile men. *Urology* 80,822–825.

Tyden T, Svanberg AS, Karlstrom PO, Lihoff L, Lampic C (2006). Female university students' attitudes to future motherhood and their understanding about fertility. *Eur J Contracept Reprod Health Care*, 11:181–189.

Uadia PO, Emokpae AM (2015). Male infertility in Nigeria: A neglected reproductive health issue requiring attention. *J Basic Clin Reprod Sci*, 4:45-53.

Vaamonde D, Da Silva-Grigoletto ME, Garcia-Manso JM, Barrera N, Vaamonde-Lemos R (2012). Physically active men show better semen parameters and hormone values than sedentary men. *Eur J Appl Phys.* 112:3267–3273.

Van Heertum, K. and Rossi, B., (2017). Alcohol and Fertility: how much is too much? *Fertil Res Pract*, 3:10.

van Oers A M, Groen H, Mutsaerts M A Q, Burggraaff J M, Kuchenbecker W K H, Perquin D A M et al.(2016). Effectiveness of lifestyle intervention in subgroups of obese infertile women : a subgroup analysis of a RCT. *Hum Reprod*, 31(12): 2704.

Varshini, J., Srinag, B.S., Kalthur, G., Krishnamurthy, H., Kumar, P., Rao, S.B., Adiga, S.K., (2012). Poor sperm quality and advancing age are associated with increased sperm DNA damage in infertile men. *Andrologia*,. 44:642-649.

Via M (2012). The Malnutrition of Obesity: Micronutrient. *Endocrinol*, 2012:1-8.

Wasiu Eniola, O. ; Adebayo Adetola, A. and Taiwo Abayomi, B. (2012) . A review of female Infertility: Important Etiological Factors and Management. *J Microbiol Biotech Res*, 2, 379-385.

Whitcomb, B., Purdue-Smithe, A., Szegda, K., Boutot, M., Hankinson, S., Manson, J., Rosner, B., Willett, W., Eliassen, A., Berton-Johnson, E., (2017). Cigarette smoking and risk of early natural menopause. *Am J Epidemiol.* 187(4):P.696-704.

Wise LA, Rothman KJ, Mikkelsen EM, Sorensen HT, Riis AH, Hatch EE (2012). A prospective cohort study of physical activity and time to pregnancy. *Fertil Steril.* 97:1136-1142.

Wright C, Milne S, Leeson H (2014). Sperm DNA damage caused by oxidative stress: modifiable clinical, lifestyle and nutritional factors in male infertility. *Reprod BioMed Online*, 28, 684– 703.

Wu FC, Tajar A, Pye SR, Silman AJ, Finn JD, O'Neill TW, et al (2008). Hypothalamic -pituitary-testicular axis disruptions in older men are differentially linked to age and modifiable risk factors: the European Male Aging Study. *J Clin Endocrinol Metab*, 93:2737–2745.