Reproduction & Risk Factor Awareness : A Review

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Abstract

Infertility is a global phenomena that affects people worldwide. In our society child bearing and motherhood defines a woman's identity. Hence, the social stigma of infertility impacts women heavily. Primary prevention of infertility is one of the most important factors for reducing its occurrence. Life-style factors, such as delayed marriage and delay in child bearing on account of education and career, stress, obesity, smoking and alcohol use, sexually transmitted infections, menstrual irregularities and environmental pollutants, have been increasingly found to be associated with reduced fertility. Increasing the level of knowledge of these factors may help to decrease the incidence of infertility by allowing couples to avoid certain risk factors that might lead to it. Moreover, patient education has been found to be a key aspect of patient satisfaction with infertility care. But knowledge of the causes of infertility appears to be lacking among young adults living in various developing countries. This review article focuses on the risk factors associated with infertility among the reproductive adults.

Introduction

Parenthood is a social role and the desire to have a child is a universal phenomenon. But many people don't get the chance to realize the joy of parenthood due to the infertility problem. Infertility is a global phenomenon that affects 60 to 168 million people worldwide [1]. Infertility affects one in six to seven couples. Infertility may occur due to factors in the male (20%) or female (33%) or both the sexes (39%), or due to unknown causes (8%)

[2]. Hence, evaluation of both partners is needed simultaneously. World Health Organization (WHO) defines primary infertility as inefficiency to conceive after a year of unprotected sex and secondary infertility in case of failure to conceive following previous pregnancy. According to WHO, the national prevalence of primary and secondary infertility in India is 3% and 8% respectively [3, 4]. Usually, investigations for infertility are recommended after 12 month of exposure, but may be required earlier, if female age> 35 years or there is a history of oligo/amenorrhea, pelvic surgery, tubal infection or chemotherapy.

The most common causes of male infertility are impaired sperm count, undescended testicles, testosterone deficiency, blockage of epididymis and retrograde ejaculation. The common causes of female infertility include polycystic ovarian syndrome, hormonal imbalance, fallopian tube block, fibroids, early menopause and pelvic adhesions. The importance of infertility as a public health problem affecting the individual and the family's mental and social wellbeing has resulted in its inclusion in the national program for reproductive and child health [5]. Knowledge about infertility is inadequate in many parts of the world. A global survey of almost 17,500 women (mostly of childbearing age) from 10 countries revealed that knowledge regarding fertility and biology of reproduction was poor [6]. Many women have little awareness of the period of the month in which they are most fertile and when to seek treatment [7,8]. The risk factors for infertility include smoking, obesity, alcohol consumption, advanced maternal age, sexually transmitted infections, and many others [9]. According to Bunting and Boivin et.al, knowledge about fertility issues is a core motivator for fertility problems [10]. Global surveys revealed that inadequate knowledge of women regarding fertility is the key culprit for the problem [11]. In Bunting and Boivin, et.al. study, participants also showed inadequate knowledge about risk factors associated with infertility [12].

Increasing the level of knowledge of these factors may help reduce the incidence of infertility by allowing couples to avoid certain risk factors that might lead to it. This knowledge may also help wider society to understand and empathize with the infertile couple, which may lead to a decrease in the psychological burden on those who are affected. While there is widespread acknowledgement of the importance of patient education within the infertility field, there is limited research and probe into what knowledge infertility patients actually possess and how they gain infertility related information in resource poor settings where health literacy is typically low. Moreover, patient education has been found to be a key aspect of patient satisfaction with infertility care [13, 14]. Since 1978, IVF has become a well-established treatment of infertility, but still the success rate is far below expectations despite continuous effort and newer strategies. According to HFEA 2011, clinical pregnancy rate is only 24.7% among IVF treated women. In India, infertility segment is growing by leaps and bounds. Researches exploring the knowledge, behaviors, perceptions and practices regarding infertility or certain treatment options have been carried out in developed countries, but very limited data is available on the Indian population despite high prevalence of infertility.

Risk Factors

Age and Fertility

Fertility varies among populations and declines with age in both men and women, but the effects of age are much more pronounced in case of women. For women, the chance of conception decreases significantly after the age of 35 [15]. Fertility in women peaks between 20-24years of age. Female fertility decreases with increase in age, relatively little till age 30–32 years and then declines progressively. The decline is 4–8% in women aged 25–29 years, 15–19% in those aged 30–34 years, 26–46% in women aged 35–39 years , and as much as 95% for women aged 40–45 years [15]. A Dutch study observed that the probability of a healthy live-birth decreased by approximately 3.5% per year after age 30.

There is also increased incidence of clinically recognized miscarriage rate & decreased live birth rates. The miscarriage rates in natural conception cycles are generally low before age 30 (7–15%) and rise with age, only slightly for ages 30–34 (8–21%), but to a greater extent for ages 35–39 (17–28%) and older (34–52%) [15]. Success rates of ART also decline as age increases due to decrease in numbers of retrieved oocytes and embryos, increase in embryo fragmentation rates and decreased implantation rates [15]. Studies showed that there was a lack of awareness of the significance of age for declining fertility among childless Canadian women [16] and Australian women [17] and among the university students in Sweden [18]. But Bunting and Boivinet.al., study showed that people were better aware of the relationship between age and declining fertility [12].

Obesity and Fertility

Overweight is a body weight, including muscle, bone, fat, and body water, in excess of some standard or ideal weight. Body mass index (BMI), Waist-hip ratio (WHR) and waist circumference are the parameters used to measure obesity. In women, obesity is associated with menstrual irregularities, ovulatory dysfunction, altered endometrial receptivity, decreased fertility, and increased risks of miscarriage and obstetric and neonatal complications [19]. Data from cross-sectional studies indicate 30-47% of overweight and obese women have irregular menses and non-ovulatory cycles [20].

Obesity lowers the chance of pregnancy following IVF, requires higher dose of gonadotrophins, high rate of cycle cancellation and has an increased miscarriage rate [21]. Obesity can affect fertility in both men and women. Abolfotouh et.al. [22] and Brannian et.al. [23] study also showed that obesity affects fertility in both men and women. Infertile couples were found to be more knowledgeable about this issue, possibly because of the prevalence of obesity in this group of patients. In Bunting and Boivin et.al. study [12], participants believed that healthy habit has an impact on pregnancy rates. Bunting and Boivin et.al. study [24] showed that 72.9% women were aware of the fact that a woman's weight affects her chances of conceiving a child.

Irregular Cycle and Infertility

Irregular or infrequent menses indicate ovulatory dysfunction. Prevalence of an ovulatory cycles is highest under age 20 and over age 40. Most women have cycles that last from 24 to 35 days, but at least 20% of women experience irregular cycles [15]. Normal cyclic menses result

usually from normal ovulatory function. Irregular cycle is the most common clinical manifestation of anovulation. Disorder of ovulation account for 20 – 40% cases in infertile couples. Ovulatory dysfunction may result in anovulation or oligoovulation. Ovulatory dysfunction occurs due to thyroid disease, hyperprolactinemia and PCOS disorder, obesity, ovarian failure and hypothalamo-pituitary disorders. Menstrual history alone often is sufficient to establish a diagnosis of an ovulation. In Abolfotouh et.al. [22] study, it was found that 64% women were aware that irregular cycle may be a cause for delay in pregnancy.

Effect of Dysmenorrhoea and Dyspareunia on Fertility

Dysmenorrhea (pain during menstruation), chronic pelvic pain, dyspareunia (pain during sexual intercourse), cyclic bowel or bladder symptoms, subfertility, abnormal bleeding, and chronic fatigue are the common symptoms of endometriosis [15]. Mean age at time of diagnosis of endometriosis ranges between 25 and 35 years. Prevalence of endometriosis in reproductive age women probably vary between 3% and 10%. It has been seen that 32% women of reproductive age with pelvic pain; 9–50% infertile women; and 50% of teenagers with chronic pelvic pain or dysmenorrhea have endometriosis. Classical studies suggested that 25–50% of sub-fertile women have endometriosis and 30–50% of women with endometriosis are sub fertile [25].

Fertile Period

Cycle fecundability is the probability that a cycle will result in pregnancy and fecundity is the probability that a cycle will result in a live birth. The period in regular menstrual cycle during which conception is most likely to occur is usually spans from day 10 to day 18 after the onset of menstruation. Sperm retains fertilizing ability for 72 hours but the egg is viable for only 24hours after ovulation. In irregular cycle, it is very difficult to know the time of ovulation and it needs monitoring. In addition, cycle fecundability increases with the frequency of intercourse during the fertile window [26]. As a consequence, the likelihood of conception can be maximized by increasing the frequency of intercourse beginning soon after cessation of menses and continuing to ovulation in women having regular menstrual cycles. The length of the fertile window may vary among women, altering the likelihood of success [27]. As a result, regular intercourse to optimize cycle fecundity should be recommended. Thus, it becomes all the more crucial to correctly know about the fertile period for a woman, the period when she may be trying to conceive. However, Ali.et.al [28] study finds that only 46% women were aware about it. In an Australian study, it was observed that only 32% of women correctly identified the most fertile time during the menstrual cycle [17] but Linda Rae Bennet [29] study found that 70% women were able to identify it.

Genital Tract Infection and Infertility

The second most common cause of infertility, lower genital tract infection gains access to uterus, fallopian tube and ovaries by ascending through the normally protective cervical barrier. The effects of PID further leads to tubal infertility, ectopic pregnancy, tubo-ovarian abscess and endometritis. Fallopian tubes bear the biggest brunt in the process of infertility most common infection related to infertility includes tuberculosis, chlamydia, gonorrhea, poly microbial infection

and nonspecific pelvic inflammatory disease. Early initiation of treatment may not prevent complications but can limit it from spreading further. The prevention of pelvic infection is more effective than treatment. In the Untied States, nearly 30% of lower genital tract infection leads to PID and results in infertility in 20% of cases. Post-infection tubal damage due to PID is responsible for 30-40% cases of infertility [30]. In Abolfotouch et.al. and Ali et.al. study, 50% of respondents were found to be aware of genital tract infection as a risk factor for infertility [22,28]. Since genital tract infection, diagnosis and treatment can prevent the major sequel to the tubal block, awareness of genital tract infection as a risk factor is highly required in our society.

Stress and Infertility

Stress, diet and exercise form a triad associated with chronic anovulation and hypothalamic amenorrhea. Psychological distress is found to be common in couples suffering from subfertility, which can be considered as both cause and effect of infertility [31]. Infertility may impact patients self-esteem and body image which may serve to reinforce the potentially stress-inducing notion that the individual is a patient with medical problems. In a study, the authors concluded that infertile women have different personality profile and their stress level (measured by serum prolactin and cortisol) were elevated compared to the control group [32]. Coping with stress may ultimately provide assistance to conception through stress reduction and help people reduce treatment termination. In Domar's review of the association of psychological distress and ART, outcome concludes women undergoing ART procedures report significant levels of negative psychological symptoms both prior and after an unsuccessful treatment cycle. From a psychological standpoint, women facing infertility exhibit significantly more tension, hostility, anxiety, depression, self-blame and suicidal ideation [9]. In the study by Abolfotouh et.al, 72% of respondents were aware that psychological distress affects fertility [22].

Fertility and Heredity

In general, fertility problems are not hereditary but depend on the causes of infertility. Some fertility problems are hereditary. Common causes for infertility that can in fact be hereditary are endometriosis, premature ovarian insufficiency and PCOS (Polycystic Ovarian Syndrome). Many women are unable to conceive and deliver a healthy baby due to genetic factors. Sometimes an inherited chromosome abnormality and a single-gene defect passed from parent to child results in infertility. Poor egg quality or low ovarian reserve is not generally considered to be hereditary causes of infertility. Blocked or damaged fallopian tubes are generally not hereditary.

Environmental Pollutant and Fertility

Compounds which disrupt communication between different cells affect the endocrine system, fertility and cause reproductive dysfunction called as Endocrine disrupting chemicals (EDC). EDC are thought to effect reproduction by directly or indirectly mimicking, stimulating, antagonizing, altering or displacing natural hormones. EDCs also raise prevalence of endometriosis in industrialized countries [33]. The possible mechanisms by which environment adversely influences fertility can be physical, chemical and psychosocial. Chemical mechanism is based on occupational exposure, i.e., solvents, welding,

agriculture, alcohol, smoking, caffeine, air, food and water. Pesticides, phthalates, heavy metals, polychlorinated biphenyles results in irregular menses, reduced fertility, fecundability and decreases the success rate in IVF and lengthens time to achieve pregnancy [31].

Exercise and Fertility

Women who are involved in strenuous recreational exercise or other forms of demanding physical activity, such as dance, have a high prevalence of menstrual irregularity and amenorrhea. Evidence suggests that moderate regular exercise positively influences fertility and assisted reproductive technology (ART) outcomes but high intensity exercise reduce fertility. A systematic review identified only three studies examining the effect of exercise on fertility in overweight and obese women with PCOS [34]. Compared to diet alone or no treatment, exercise helps improve menstrual function and/or ovulation frequency. A study has reported a trend for a higher pregnancy rate for exercise compared to diet (35% versus 10%, p=0.058). Studies of the effects of 12–24 week lifestyle interventions comprising diet, exercise and/or behavioral change in overweight infertile women with or without PCOS report improved ovulatory and menstrual regularity and reduced risk of miscarriage compared to pre-intervention. National and International evidence-based physical activity guidelines recommend at least 30 minutes of moderate-intensity physical activity on most and preferably all days of the week in couples seeking ART [35]. For men and women who are overweight and obese, achieving and maintaining a modest weight loss may improve fertility and improve other obesity-related morbidities. In a study by Bunting and Boivin et al., participants correctly answered that regular exercise increases the chances of pregnancy, but in Ali.et.al. study, only 13% participants were found to be aware of it [28].

Smoking and Male Infertility

In males, it has been suggested that cigarette smoking negatively affects every system involved in the reproductive process and epidemiological data indicate that up to 13% of infertility may be attributable to cigarette smoking. Gamete mutagenes is is one possible mechanism whereby smoking may adversely affect fecundity and reproductive performance. Spermatozoa from smokers have reduced fertilizing capacity and embryos display lower implantation rates. Different articles have demonstrated a negative impact of smoking on human semen parameters, correlated with cigarettes smoked per day and the smoking duration. Nicotine has a significant influence on sperm morphology and sperm count. Most of the reports agreed that smoking reduces sperm production, sperm motility, sperm normal forms and sperm fertilizing capacity through increased seminal oxidative stress and DNA damage. There is ample evidence [36] to suggest that semen parameters and results of sperm function tests are 22% poorer in smokers than in nonsmokers and the effects are dose-dependent, but smoking has not yet been conclusively shown to reduce male fertility. In studies by Bunting and Boivin et.al., [12] and Daniluk and Koert study [16], women participants said that they think smoking reduces the sperm parameters.

Age and Male Fertility

There is modest age-related decrease in semen volume, sperm motility and morphologically normal

sperm count but not sperm density [15]. In studies of the effect of male partner age on pregnancy rates, female partner age and declining coital frequency with increasing age are obvious and important confounding factors. A British study (adjusting for the confounding effects of both partner's age and coital frequency) found that increasing men's age was associated with increasing time to conception and declining overall pregnancy rates; time to conception was 5-fold greater for men over age 45 than for men under age 25 [15]. Sperm chromosomal abnormalities may increase with age and adversely affect early embryonic development. There is at least some evidence to suggest that increasing male age may raise the risk of miscarriage in young women. Rise in FSH levels in men towards 30 years, suggesting age-related changes in the hypothalamic-pituitary-gonadal axis [15]. The testes and prostate also exhibit morphological changes with aging that might adversely affect both sperm production and the biochemical properties of semen. It has been seen that there is decrease in pregnancy rates and increase in time to conception with the increase in male age. But there is little or no overall measurable decline in male fertility before age 45–50, and male factors generally contribute relatively little to the overall age-related decline in fertility [37]. Daniluk and Koert et.al study shows that increase in man's age reduces the chances of fertility [16].

Secondary Infertility

If a woman has previously conceived but is subsequently unable to conceive despite cohabitation for at least 12 months, then she is said to have secondary infertility. According to demographic and reproductive health survey, prevalence of secondary infertility in India is 24.6% [30]. Most couples don't think infertility can occur with people who already have kids. But the truth is that this problem is quite common and growing in our country. Pelvic adhesions caused by endometriosis or previous MTP following first pregnancy or previous abdominal surgeries or hormonal disruption/imbalance after the first pregnancy could also cause secondary infertility.Tubal damage (scarring and adhesion leads to tubal occlusion) which mainly occurs due to upper genital tract infection is the common cause of secondary infertility [31]. Post abortal or puerperal sepsis can lead to tubal damage and peritubal adhesion leading to secondary infertility. Infection with Chlamydia trachomatis, Neisseria gonorrhoea and genital tuberculosis are the high-risk factors for tubal damage [15].

Conclusion

Infertility is a fairly common problem affecting10–15% of the population. Knowledge about fertility issues is a core motivator for seeking treatment for fertility problems. Global surveys revealed inadequate knowledge of women regarding fertility. Although there is a wide spread acknowledgement of the importance of patient education within the infertility field, there is limited research into the knowledge which infertile patients actually possess and also the way they gain infertility related information in resource poor settings where health literacy is typically low. Since the prevalence of infertility is on the rise due to late marriages, delay in child bearing in carrier oriented women, stressful and altered life styles, increasing the level of knowledge of these factors may help to decrease the incidence of infertility by allowing couples to avoid certain risk factors that might lead to it.

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Our Vision

Harmonious existence between male and female leading the mankind towards ultimate bliss

Our Goals

INDIAN INSTITUTE OF SEXOLOGY BHUBANESWAR (IISB)

- *Aims to facilitate the integration of knowledge and expertise across various disciplines like medicine, psychology, sociology, law and ethics for greater understanding of complexities of human sexuality*
- *Aims to adequately address the individual sexual problems and social issues*

Objectives

- *To bring experts of different disciplines to a common platform for sharing of knowledge and views on human sexuality*
- *To promote research on human sexuality*
- *To impart training on 'Sexology' and strengthen the discipline of 'Sexual Medicine'*
- *To encourage medical professionals to choose 'Sexual Medicine' as a career*
- *To create public awareness on human sexuality and gender issues*
- *To advocate any social change for betterment of mankind*