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Review Article

Infertility: A Review on Causes, Treatment and Management

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Abstract

For healthy young couples, the likelihood of getting pregnancy varies. In 2010, an estimated 48.5 million couples worldwide were infertile [1]. This paper provides a review on infertility causes, investigations, treatment modalities and role of nurse midwife in dealing with infertile couples. Infertility (a state of subfertility) can be manifested either as the inability to become pregnant, inability to uphold a pregnancy, and inability to continue a pregnancy till term [2,3]. There are various causes of female and male infertility. A vast number of investigations can be done to rule out the exact cause of infertility both in males and females. There are various treatment modalities that may be useful for the infertile couples. Although, for infertility treatment, couples visit gynecologists, but along with them the nurse midwives' play an important role to help the couple explore and identify problems related to reproductive health and coordinate with multidisciplinary team to promote and maintain reproductive health.

Keywords: Infertility, Subfertility, Ovulation, Implantation, Role of midwife/ nurse

Introduction

Infertility is defined as the inability to conceive naturally after one year of regular unprotected intercourse. Most of the time, infertility is some degree of subfertility in which 1 in 7 couples need specialist help to conceive. Subfertility can be either primary or secondary. Primary subfertility is a delay for a couple who have had no previous pregnancies; and, secondary subfertility is a delay for a couple who have conceived previously, although the pregnancy may not have been successful for example, miscarriage, and ectopic pregnancy [4]. The aim of this paper is to discuss the male and females causes of infertility, treatment modalities and role of midwife in dealing with infertile couples.

The chance to conceive depends on the length of sexual exposure, frequency of coitus, and couple's age. The normal, young aged couples have a 25% chance to conceive after 1 month of unprotected intercourse; 70% of the couple's conceive by 6 months, and 90% of the couples have a probability to conceive by 1 year. Only 5% of the couples will conceive after one and a half year or two years [5,6].

Both males and females are equally responsible for the causes. Most of the infertile couples have one of these three major causes including a male factor, ovulatory dysfunction, or tubal-peritoneal disease [5]. Literature shows that vaginismus and dyspareunia are more common in 20-24 years aged females [7].

The sexual response cycle plays an important role to promote fertility, because it comprises of sequential physical and emotional changes that occur as a person becomes sexually aroused [8]. In normal physiology, the two gonadotropin hormones, follicle stimulating hormone (FSH) and luteinizing hormone (LH) are produced in the pituitary and their secretion is controlled by gonadotropin releasing hormone (GnRH) that is released by the hypothalamus. At the start of a new cycle, the hypothalamus begins to release GnRH that acts on the pituitary gland to release FSH and LH. These two hormones stimulate the ovary and cause the follicles to develop. Every month about 30-40 follicles start to grow in response to FSH, but only a single mature egg is released every month. This involves messages transmission in the form of hormones from the ovary, the pituitary and the hypothalamus. When the egg is ripe, the mature follicle releases an increasing amount of estrogen, is produced by the granulosa cells lining the follicle. The estrogen produced by the dominant follicle progressively increases in quantity as the egg matures, until a surge of estrogen is released into the blood. The high level of estrogen stimulates the pituitary to release a large amount of LH, thus leading to

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the LH surge. This LH in turn acts on the mature follicle, causing it to rupture to release the mature egg (ovulation) in the ovary [8].

Males born without testes or vas deferens can become infertile. Some men have both the testes but they are not able to produce sperm or may produce very few sperms also suffer from infertility. Moreover, stress can cause decreased libido and the couple can end up in having infertility.

Causes of Female Infertility

According to the Center of Disease Control (CDC, 2013) [9], the causes of female infertility can be divided into three broad categories including defective ovulation, transport and implantation. These categories are further discussed below in detail.

Defective Ovulation

Defective ovulation occurs because of the following causes:

Endocrine disorders: The dysfunction of hypothalamus and pituitary gland can lead to an excess amount of prolactin, this may prevent ovulation. Moreover, other endocrine glands including adrenals and thyroid may also delay ovulation. When the corpus luteum, fails to produce enough progesterone required to thicken the uterine lining, the fertilized egg may not be able to implant, thus leading to infertility.

Physical disorders: Certain physical disorders such as obesity, anorexia nervosa, and excessive exercise may lead to overweight or malnutrition, and later the menstrual cycle, thus make the couple infertile.

Ovarian disorders: Polycystic ovarian disease (PCO) can lead to infertility because of an increased amount of testosterone and LH and decrease uptake of glucose by muscle, fat and liver cells resulting in the production of large amounts of insulin by the pancreas. Low FSH levels also hinder the production of eggs from the ovarian follicles, and lead to form fluid-filled ovarian cysts that eventually cover the whole ovaries and prevent conception.

Endometriosis: This refers to a condition in which sections of the uterine lining implant in the vagina, ovaries, fallopian tubes or pelvis. These implants form fluid- filled cysts that grow with each menstrual cycle, and eventually turn into blisters and scars. These scars then block the passage of the egg and delay pregnancy.

Defective Transport

The following can lead to defective transport of ovum and sperm:

Ovum: Occurrence of Pelvic Inflammatory Disease (PID), gonorrhea, peritonitis, previous tubal surgery, and fimbrial adhesions can cause tubal obstruction; as a result the egg is not released or trapped, therefore, delaying conception.

Scar tissue after abdominal surgery: After abdominal surgeries, presence of scar tissue may alter the movement of the ovaries, fallopian tubes, and uterus, resulting in infertility.

Sperm: Presence of psychosexual problem such as vaginismus, or dyspareunia may hinder fertilization and make the couple infertile.

Cervix: Trauma, surgery, infection, anti-sperm antibodies in the cervical mucus may also delay pregnancy.

Defective Implantation

Defective implantation can occur because of the following causes:

Congenital anomaly and fibroids: Congenital uterine anomaly such as bicornuate uterus and uterine fibroids near the fallopian tubes or cervix may alter implantation of the zygote and cause infertility.

The causes of female infertility are discussed, and now the paper reviews the male causes.

Causes of Male Infertility

According to the CDC (2013), male causes of infertility are divided into the following four main categories:

Defective Spermatogenesis: Presence of endocrine disorders such as diabetes mellitus and hyperthyroidism lead to azospermia or the formation of faulty sperms that are not capable to fertilize the ovum. Moreover, testicular disorder such as undescended testis can also affect fertility.

Defective Transport: Obstruction of the seminal vesicles or absence of the seminal ducts may affect the mobility of the sperms, and thus end up in infertility.

Ineffective Delivery: The psychosexual problems like impotence, ejaculatory dysfunction, physical disability, hypospadias, and epispadias can affect fertility of males.

After discussing both male and female causes of infertility, this paper further states the history and physical examination component.

History and Physical Examination

To assess and evaluate couple's condition, a midwife should take a detailed history and perform physical examination [4].The following history should be taken:

- How long you have been trying to conceive?
- How often do you have sexual intercourse?
- Are there any problems with intercourse?
- Has there ever been conception even if the outcome was miscarriage?

In terms of general health, the midwife should explore the menstrual history of the female including age of menarche, duration and amount of menstrual flow, presence of dysmenorrhea and dyspareunia. A thorough history of male should be explored regarding impotence, premature ejaculation, and psychosexual problems. Moreover, questions related to systemic diseases including thyroid, PCOs, diabetes should be asked. Also, explore history of drugs use such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs); as these drugs may impair ovulation. It is crucial to review the past surgical history in both male and female. The midwife should ask for appendectomy or any pelvic surgery in female, whereas in male it is necessary to ask about testicular trauma and undescended testes.

Pertaining to physical examination, assess the following:

- Weight and Body Mass Index (BMI), if BMI is <20 it may suggest an-ovulation as in anorexia nervosa; and if the BMI is >29 it may be because of PCOs leading to decreased fertility.
- Assess for the presence of acne and hirsutism, as this could be because of high levels of androgen.

Following examinations may also be done to correlate the findings with the clinical features:

- In female, abdominal and bimanual pelvic examination can be done to rule out ovarian cyst, tenderness due to endometriosis or PID, and uterine fibroids.
- Per vaginal examination may suggest vaginismus, and the midwife may find an intact hymen. In addition, a large clitoris may suggest excessive androgen activity; therefore, a pap smear may be suggested.
- Transvaginal scan can be done to assess the anatomical structure of the reproductive organs.
- Male sexual examination should be done to assess penis appearance, if, hypospadias is present, then semen may deposit away from the cervix in the acidic area of the vagina where the spermatozoa become immobilized and inactive.
- Check testes size and consistency, rule out whether descended or undescended, and also rule out inguinal hernia.

Investigations

The following investigations can be done to confirm the diagnosis in female:

I. Female Endocrine System Evaluation

Basal Body Temperature Charting (BBT): This is the simplest test for ovulatory evaluation. Elevated progesterone levels during the second half of the menstrual cycle cause the temperature of the body to rise 0.5-1.0 0F. A BBT chart which demonstrates a 12 to 14 day elevation in temperature after day 11-16 is considered to be normal. Approximately 90% of women can be expected to have ovulated two days before or after the lowest temperature recorded before a sustained rise.

Endometrial Biopsy: An endometrial biopsy in the mid to late luteal phase (post-ovulatory day 7 to 12) can provide the confirmatory information to the BBT and serum progesterone testing, as well as diagnose endometritis. It is the gold standard for diagnosing luteal phase defect. Multiple endometrial biopsies are not necessary to monitor response to ovulatory drugs.

Urinary Luteinizing Hormone Detection: This predicts LH surge, the urinary LH surge usually occurs about one to two days prior to the rise in BBT and 12 to 60 hours before ovulation. A shorter range is 22 to 44 hours, with a mean of 30 hours. The most sensitive use of the test requires a woman to empty her bladder in the morning, restrict fluids, and then perform the test between 10 AM and 12 PM.

Ultrasonography: It can be performed either trans-abdominally or, preferably, trans-vaginally, and is a very useful clinical tool to evaluate follicular development and ovulation. As discussed earlier, generally follicles mature and rupture between 17 to 22 mm in size. The loss of follicular size, the loss of clear follicles, and the appearance of fluid in the cul-de-sac are all suggestive of ovulation. The presence of multiple small follicles is indicative of PCO.

Additionally, endometrial thickness in the mid luteal phase greater than 8 mm reflects of normally developed post ovulatory endometrium.

Follicle Stimulating Hormone (FSH) and Estradiol (E2)

The normal upper range for this test is generally 10-13 mIU/ml. Levels below this range are normal, while levels approaching 20 mIU/ml are associated with markedly decreased pregnancy rates. E2 is almost always tested at the same time as the FSH level to prevent an inappropriate interpretation of the test results. Several studies have demonstrated that even one elevated cycle day 2-4 FSH level is associated with a poorer prognosis

Laparoscopy: This may be performed to identify ovarian follicles and irregularities related to normal ovulation. The finding of a follicular cyst on the ovary or corpus luteum is suggestive of ovulation. The presence of multiple small follicles confirms the presence of PCO.

II. Pelvic Factor Investigation

If a gynecologist and a midwife suspect a physical or anatomic problem within the women's pelvis, the following diagnostic tests can be conducted:

Hystero-salpingogram (HSG): It is a procedure in which a small amount of radio-opaque fluid is injected into the uterus and fallopian tubes and then visualized with x-rays. It is useful to diagnose intrauterine structures and lesions and evaluate status of the tubes in the proximal, distal, and intra-pelvic region. Additionally, data suggest that the HSG may be associated with increased rates following its use. Disadvantages of HSG include pain and discomfort, radiation exposure, infection, dye embolism and iodine hypersensitivity.

Hysteroscopy: This is an operative procedure performed as a diagnostic procedure or as a therapeutic intervention used to do tubal catheterization to open the blocked tubes, and, visualize the internal structure of the tubes. This diagnostic test may be very useful in determining the functional status of the fallopian tubes. Disadvantages of the procedure include adhesions and potential surgical and anesthetic complications. Scarce evidence on the effectiveness of hysteroscopic surgery in sub-fertile women with polyps, fibroids, septate/ bipartite uterus or intrauterine adhesions exist, therefore, it is suggested to conduct Randomized Control Trials (RCTs) to provide general recommendations [10].

Magnetic Resonance Imaging: This can be useful for differentiating myomas, and complex congenital uterine and pelvic abnormalities as well as masses. Its high cost limits its general use, but it is helpful in selected situations.

III. Cervical Factor Investigation

If gynecologist and midwife suspects that the source of infertility may be related to the interactions of the cervical

mucus with the sperm, then the following investigations can be performed:

Post-Coital Test: This is the standard test for evaluating cervical factor infertility. The test can help to identify difficulty in timing intercourse, sexual dysfunction, poor cervical mucus, cervical infection, low sperm count and/or motility, and the presence of antibodies; but this test is not very accurate. It must be carefully timed to be performed at ovulation or the results are not interpretable.

Antisperm Antibody Tests: Antisperm antibody tests may be helpful in selected patients with shaking sperm motion on the semen analysis or post-coital test, or a history of testicular operation or injury.

Cervical Cultures: Cervical cultures can be assessed for E. coli, gonorrhea, chlamydia, and mycoplasma can be helpful in identifying infection in selected patients or in those undergoing intrauterine insemination or assisted reproductive technology procedures.

In Male

Male infertility is mostly related to deficiencies in sperm transport or spermatogenesis. Diagnosis can be confirmed by doing a detailed evaluation of semen analyses, gonadotropin and other assays [11].

Semen Analyses: This should be done and the midwife should explain the procedure to collect specimen. Semen should be produced by masturbation, after three days of abstinence from sexual activity. The specimen should be kept warm and sent to laboratory, within an hour from production.

Sperm function tests: These tests can be done to evaluate the function of the sperms. The Hamster Egg Penetration Assay (HEPA) and the Hemizona Assay (HZA) can help to assess the ability of sperm to penetrate the egg.

FSH and LH: The levels of FSH and LH can be raised in a condition called hyper gonadotrophic hypogonadism. In this condition, the high levels of FSH and LH occur due to impaired spermatogenesis as a result of testicular failure. Moreover, clients with cryptorchidism, Klinefelter's syndrome, orchitis, testicular torsion, testicular tumor, etc. can also have this problem and become infertile. Whereas, in hypo gonadotrophic hypogonadism, the levels of FSH and LH are decreased due to pituitary gland or hypothalamus dysfunction. Clients with Kallmann's syndrome, malignant CNS tumors, pituitary adenoma, etc. can suffer from this condition and become infertile.

Urine analyses: Untreated urinary tract infections and sexually transmitted diseases can also cause infertility. It is important to evaluate such infections. These infections can also cause partial or complete obstruction of the ejaculatory ducts, prostate gland and seminal vesicles.

Color Doppler Ultrasound: To evaluate intra-scrotal defects, Doppler ultrasound can be done to detect varicocele, testicular tumors and testicular micro-calcifications.

Testicular biopsy: Testicular biopsy is often done in clients with azoospermia, but having normal testicular volume and FSH levels. This is performed in clients who decide to go for Intracytoplasmic Sperm Injection (ICSI).

Apart from this, these additional tests can also be done for men with azoospermia such as: seminal plasma fructose, this can be done to assess the status of vas deferens; urethral cultures can be taken to rule out infection, and serum FSH, testosterone, and prolactin can be evaluated to rule out sexual dysfunction. Karyotype is indicated when there is suspected chromosomal abnormality (CDC 2013).

Treatment Modalities

Infertility treatment depends on the cause, duration, both partners age, and personal preferences. The couple should be explained that some of the causes of infertility cannot be corrected. Financial, physical, and time commitment is required for infertility treatment. The following treatment modalities can be explained to the couple after assessing and evaluating the couple's health:

Intra-uterine Insemination (IUI): This could be used for unexplained infertility and female cases with minimal endometriosis and mild male factor infertility problems. In this, healthy sperms that have been collected and concentrated are placed directly in the uterus around the time of ovulation. The timing of IUI can be coordinated with the normal cycle or by using fertility medications.

***In-Vitro* Fertilization (IVF):** In IVF, multiple mature eggs from a woman are retrieved, and fertilized with a man's sperm outside the womb and inside a laboratory. Then, the fertilized embryos are implanted in the uterus after three to five days of fertilization.

Zygote Intra-fallopian Transfer (ZIFT) and Gamete Intra-fallopian Transfer

(GIFT): In ZIFT, the fertilized egg is directly transferred into the fallopian tube; whereas, in GIFT a mixture of sperms and eggs is placed in the fallopian tube and fertilization occurs there.

Intracytoplasmic Sperm Injection (ICSI): In ICSI, a single healthy sperm is injected directly into a mature egg. ICSI is used when there is a problem with the quality of the semen, or there are few sperms, or prior IVF cycles have failed.

Assisted Hatching: Through this technique, implantation of the embryo into the uterus is assisted by breaking the outer covering of the embryo. This helps the embryo to smoothly implant

Donor Eggs and Sperms: Assisted reproductive technology mostly uses the married couple's eggs and sperms, but when there are severe issues with the eggs and sperms then donor sperms or even embryo is taken to enhance fertility.

Gestational Carrier: This is sometimes called as surrogate pregnancy, when a woman who does not have a uterus or if the uterus is not functional and to whom the pregnancy can endanger health, the couple can decide to have a gestational carrier, who carries the couple's embryo in the uterus.

Adoption: This can be an option for couples who have multiple unexplained IVF failure cycles.

Role of Nurse Midwife

Although, infertile couples consult gynecologists for treatment,

but, the first care provider who comes in contact with the couples is a nurse midwife. Nurse midwives are responsible to provide holistic care to the couples having infertility problems. Hence, it is important that they should know their role while taking care of infertile couples. The concept of care can be applied by using a number of theoretical frameworks, such as the Kolcaba Theory of Comfort to plan care. The Kolcaba Theory of Comfort considers patients to be individuals, families, institutions, or communities in need of health care. The environment is any aspect of the patient, family, or institutional surroundings that can be manipulated by a care provider or loved one in order to enhance comfort. Health is considered to be optimal functioning in the patient, as defined by the patient, group, family, or community. Nursing is described as the process of assessing the patient's comfort needs, developing and implementing appropriate nursing care plans, and evaluating the patient's comfort after the care plans have been carried out.

Comfort theory in nursing is characterized by four general contexts that encompass all aspects of patient comfort: physical, psycho-spiritual, environmental and social. Kolcaba described comfort existing in three forms: relief, ease, and transcendence. If specific comfort needs of a patient are met, the patient experiences comfort in the sense of relief; ease addresses comfort in a state of contentment; transcendence is a state of comfort in which patients are able to rise above their challenges.

The table below discusses about the care of infertile couple by using the Kolcaba Theory of Comfort (Table 1).

Relief	Ease	Transcendence
Physical		
Dyspareunia; knowledge deficit; preparation for treatment	Cyst; endometriosis, UTI, STI	Sexual dysfunction
Psycho- Spiritual		
Fear	Altered coping; anxiety	Feeling of inadequacy; grief; hopelessness; spiritual distress; loneliness
Environmental		
Injury	Environmental triggers	Safe and respectful environment
Socio-Cultural		
Cultural pressures	Social isolation; altered social interaction	Financial, social and cultural issues

Table 1. Care of infertile couple by using the Kolcaba Theory of Comfort.

Conclusion

Infertility can have drastic effects on couple's lives; hence, it is important to improve their reproductive health issue. Among other health care professionals, nurse midwives can be one of the care providers to whom the couples meet initially for history taking and initial assessment. As being involved in reproductive health, they can play a vital role in infertility care also by strengthening their knowledge and competencies. They can use a number of assessment strategies, one of which is the application of nursing theories into care. They should build rapport and assess couples comfort level to share their highly personal and sensitive information. They should be knowledgeable about reproductive anatomy and physiology, and should have experience in dealing with such clients. They must have skills to help the couple to explore their fears, anxieties, feeling of hopelessness, loneliness and psychological and spiritual distress related to their sexual dysfunction, and assist in identifying coping strategies to maintain a healthy reproductive life. They can liaison between the infertile couple and the multidisciplinary health care team to identify treatment modalities to promote health as a whole with special focus on reproductive health.

References

1. Mascarenhas MN, Flaxman SR, Boerma T, Vanderpoel S, Stevens GA. National, regional, and global trends in infertility prevalence since 1990: A systematic analysis of 277 health surveys. *PLoS Med.* 2012;9(12):e1001356.
2. World Health Organization. Infertility. 2013.
3. WHO. Sexual and reproductive health. 2013.
4. Taylor A. Extent of the problem. *ABC of subfertility.* 2003;327(7412):434-436.
5. Kakarla N, Bradshaw K. Evaluation and Management of the Infertile. *Glowm.* 2008.
6. Kamel RM. Management of the infertile couple: an evidence based protocol. *Reprod Biol Endocrinol.* 2010;8:21.
7. Tayebi N, Ardakani SMY. Incidence and prevalence of the sexual dysfunctions in infertile women. *European Journal of General Medicine*. 2009;6(2):74-77.
8. Fraser DM, Cooper MA. Myles text book for midwives, 15th ed. *Churchill Livingstone Elsevier.* 2009.
9. Centers for Disease Control and Prevention. *Infertility FAQs.* 2013.
10. Bosteels, Weyers S, Puttemans P, et al. The effectiveness of hysteroscopy in improving pregnancy rates in subfertile women without other gynecological symptoms: a systematic review. *Hum Reprod Update.* 2010;16(1):1-11.
11. Jungwirth A, Diemer T, Dohle GR, et al. Guidelines for the investigation and treatment of male infertility. *Eur Urol.* 2012;61(1):159-163.