SECTION- 1

REVIEW OF LITERATURE
Introduction

Reproduction is one of basic instinct of human beings. For the fertility process to proceed smoothly, both the man and the woman should be healthy and normal. Infertility is defined as the condition in which a couple seeking for a child cannot conceive even after 12 months of unprotected intercourse (Mueller and Daling 1989; Thonneau et al., 1991). Sterility means that one can never conceive and carry a child. It is almost an irreversible condition under ordinary circumstances. Infertility and sterility do not change one's ability or desire to procreate. Sterility is the permanent inability of either a male or female to produce offspring; in a woman it is an inability to conceive; in a man it is an inability to impregnate (Habbema et al., 2004). Similarly sub-fertility generally describes as any form of reduced fertility with prolonged time for conception (Gnoth et al., 2005). It is a milder version of infertility which is reversible to fertility with or without medical help. Both infertility and sub-fertility are defined as the inability to conceive after a certain period of time (the length of which vary), so often the two terms overlap (Gnoth et al., 2005).

Incidence and prevalence of Infertility

The incidence of male infertility varies greatly. In Western countries one in four men consulting fertility clinics has specific condition like low sperm count, motility or/ and abnormal morphology, causing infertility (Bhasin et al., 1994). According to a study conducted by World health organization (WHO) regarding the diagnosis and management of male infertility (WHO, 1987), it was reported that in 20% of couple with infertility, the problem could be attributed predominantly to the male. Seshagiri (2001) has reported the incidence of infertility globally to be 13 to 18% and the male factor to be responsible in one half of the cases. Speroff (1999) has
reported 40 to 50% of infertility to be due to male factor. According to Johnson et al. (1994) about 15% of all married couples are burdened with infertility and the male contributing in 40 to 50% of the cases.

However, the incidence of male sub-fertility or infertility is not yet clear, though it is estimated that approximately 13 to 19 million couples are infertile (Sharma et al., 2005). An estimated 15% to 20% of couples meet this criteria and are considered infertile, with approximately 40% due to female factors alone, 50% due to male factors alone, 10% due to a combination of female and male factors, and unexplained factors. Globally, the incidence of infertility is estimated to be about 13–18% (Hull et al., 1985; Mueller and Daling 1989; Thonneau et al., 1991; Jones and Toner, 1993; Irvine, 1996) in the human population, regardless of race, ethnic group, etc. Aetiologies of male infertility are still generally underestimated, ignored under diagnosed and under treated. Nearly 7.5 to 10% of all men in the reproductive age group are infertile and are incapable of fathering children. According to a report conducted by the International Institute of Population Sciences, infertility is growing at an alarming pace, especially in the urban area. Out of around 250 million individuals estimated to be attempting parenthood at any given time, 13 to 19 million couples are likely to be infertile (Forest, 2004).

**Incidence of infertility in India**

The recent growth of the Indian population has been unprecedented. It stands currently at over one billion and is expected to touch 2 billion by 2035 assuming an average growth rate of 2% (Seshagiri 2001). Even though curtailing population growth is a major national concern, a substantial number of infertile couples in the Indian population have an equally great concern, that of having a child. This is an equally
important national problem concerning reproductive health and the infertile couples have to be treated by Medically Assisted Reproductive Technology (MART) for procreation (Seshagiri2001). A report showed that in India, 13% of married women aged 15-49 years were childless in 1981 (rural 13.4% and urban 11.3%) which increased to 16 percent in 2001 (rural 15.6% and urban 16.1%) (Palatty et al., 2012). Therefore over half of married women aged 15-19 years were childless in 1981, which increased to 70% in 2001. Nearly 30 million couples in the country suffer from infertility, making the incidence rate 10% (Palatty et al., 2012).

**Types of Infertility:**

Infertility can be classified as primary and secondary infertility. Primary infertility is when a couple have never had children, or unable to achieve pregnancy even after one year despite having unprotected sexual intercourse (WHO, 1983), whereas secondary infertility is when a couple have had children or achieved pregnancy previously, but are unable to conceive at second time, even after having unprotected sexual intercourse for one year (WHO, 1983). Secondary infertility occurs more commonly than primary infertility, especially in developing countries where sexually transmitted infections are common. About 67–71% and 29–33% of patients have primary and secondary infertility, respectively (Mueller and Daling, 1989; Thonneau et al., 1991; Irvine, 1996). In many countries, induced abortion contributes much too secondary infertility, which accounts for 60% of the total number of infertile cases (WHO, 1983). Idiopathic infertility is a condition of couples unable to conceive for more than two years, with no abnormalities seen on repeated investigations of tubes or as regards ovulation, luteal phase, cervical mucus, semen, sperm–oocyte interaction or intercourse (WHO, 1983).
Male infertility

Compared to other species, human males have relatively poor sperm producing capacity and human testicular function is very sensitive to a wide variety of environmental insults. This may be related to the human (upright) posture and hydrostatic pressure on venous testicular outflow, or other unknown factors, but it is necessary for clinicians to be aware of the high incidence of sub fertility in men. Perhaps it is a reflection of the incredible ability of humans to adapt the environment to promote their own survival or the expectation that fertility should be nearly spontaneous, but many human couples seek evaluation for infertility (Glover and Barratt, 1999).

The human male reproductive system includes the hypothalamo-pituitary-testicular Hormonal axis as well as the reproductive organs such as Testis, epididymis, vas deferens, seminal vesicles, prostate and urethra. Production of spermatozoa requires approximately 3 months from the initial mitotic divisions through the myriad changes readying sperm for ejaculation and fertilization. Highlights of this transformation include (1) the unique environment created within the testis for spermatogenesis to occur; (2) preservation of a set of stem cells relatively resistant to external injury and able to produce rapidly proliferating germ cells destined to become spermatozoa; (3) meiosis, that results in formation of the haploid gamete; and (4) the dramatic differentiation of the prospective gamete in a form that is specialized to transport chromosomal material in a structure ideally suited for transit of the female reproductive tract. The spermatozoa resulting from this complex process assumes its final shape and size in the testis. In the normal state, it also acquires the ability to fertilize as well as a capacity for motility in the epididymis. Unfortunately, the mechanisms by which the epididymis exerts these changes on the
traveling spermatozoon and the actions of the human reproductive tract after relief of chronic obstruction remain largely unknown (Glover and Barratt, 1999).

**Etiology of male infertility**

The etiology of the male infertility is multifactorial and still little is known about the causative factors dealing with impaired spermatogenesis. Male infertility has been associated with several genetic and non-genetic conditions (Poongothai *et al.*, 2009). Among the major causes of infertility, chromosomal abnormalities, microdeletions, cystic fibrosis transmembrane conductance regulator (CFTR) mutations and other genetic factors [follicle stimulation hormone (FSH) receptor mutation] are important (Irvine, 1996; Phillip *et al.*, 1998; Diemer and Desjardins, 1999; Egozcue *et al.*, 2000; Hargreave, 2000). Anatomical abnormalities such as varicocele, vesicular damage due to torsion and obstruction of testicular sperm passage can all lead to male infertility. The known causes of male infertility are quite numerous but can be grouped into a number of major categories. Non-obstructive azoospermia has a strong genetic basis where there is an excess existence of autosomal abnormalities (Hargreave, 2000). Besides, congenital bilateral absence of the vas deferens (CBAVD) associated with the phenotype of CFTR gene mutations cause obstructive azoospermia (Donat *et al.*, 1997). It is unclear that up to what extent genetic contributes. It has been reported that in a certain ethnic group, men with a particular haplotype (II) have a lower sperm concentration compared with men with haplotypes (III) and (IV) and, the frequency of haplotype (II) is more common in azoospermic men compared with normal men (Kuroki *et al.*, 1999). Based on this, it appears that the genetic contribution towards male fertility on account of a decreased sperm concentration might be significant in some ethnic groups. There are a number of nongenetic risk factors such as Sexual Transmitted Diseases (STD s) involving N.
gonorrhoeae and C. trachomatis. These cause changes semen quality and chronic infection may lead to a block of the vas deferens or seminal vesicles (Megory et al., 1987). Mumps, though rare in adults, can result in azoospermia.

Besides, immunological factors operate at almost every step in the human reproductive process, antibodies induced damage to gametes and developing embryos is a major cause of immunological infertility (Carlsen et al., 1992). There appears to be a world-wide concern over decreasing human sperm concentration but this has been highly controversial. Decreasing sperm counts are attributed to the deleterious effects of environmental contamination by heavy metals and estrogenic chemicals (Mehta and Anandkumar, 1997; Benoff et al., 2000; Sharpe, 2000). Life style, environmental factors (Benoff et al., 2000; Sharpe, 2000), including smoking (Zenzes 2000), can also affect gamete and embryo development, leading to subfertility or infertility. A combined cause of infertility is found in about 10–30% of couples (Hull et al., 1985; Thonneau et al., 1991; Jones and Toner 1993). In addition to these causes, another important category is unexplained male infertility (UMI) or idiopathic male infertility that is reserved for infertile males with unknown origin factors with normal semen parameters in which female partner infertility factors have been ruled out. It ranges from 6 to 27% (Moghisis and Wallach, 1983; Sigman et al., 2009).

**Anatomy and pathology of Human male reproductive system:**

The human male reproductive system consists of a number of sex organs that form a part of the human reproductive process. The male sex organs can be classified as External genital organs and Internal Genital organs. The main external genital organs are the penis, testes and epididymis. Testis produce semen and sperm, which, as part of sexual intercourse, fertilize an ovum in the female’s body; the fertilized
ovum (zygote) develops into a fetus, which is later born as a child. In this type of reproductive system, these sex organs are located outside the body, around the pelvic region. The main male internal genital organs are vas deferens, seminal vesicles and prostate.

**External genital organs**

**Penis:** The penis is the male copulatory organ. It has a long shaft and an enlarged bulbous-shaped tip called the glans penis, which supports and is protected by the foreskin. When the male becomes sexually aroused, the penis becomes erect and ready for sexual activity. Erection occurs because sinuses within the erectile tissue of the penis become filled with blood. The arteries of the penis are dilated while the veins are passively compressed so that blood flows into the erectile cartilage under pressure (Figure 1). The human penis differs from those of most other mammals, as it has no baculum, or erectile bone, and instead relies entirely on engorgement with blood to reach its erect state. It cannot be withdrawn into the groin, and it is larger than average in the animal kingdom in proportion to body mass (Poncheietti *et al.*, 2001).

**Disorders of penis:** Many disorders are associated with penis such as Penile hypoplasia, Hypospadiasis, Phimosis, Paraphimosis, Peyronie's disease, Pudendal nerve entrapment, Penile fracture, Erectile dysfunction, etc. Thrombosis can also occur during periods of frequent and prolonged sexual activity, especially fellatio. Infection with the herpes virus can occur after sexual contact with an infected carrier; this may lead to the development of herpes sores. In diabetes, peripheral neuropathy can cause tingling in the penile skin and possibly reduced or completely absent sensation. Priapism is a painful and potentially harmful medical condition in which the erect
penis does not return to its flaccid state. Potential complications include ischaemia, thrombosis, and impotence. In serious cases the condition may result in gangrene, which may necessitate amputation (Goldenberg, 1998). Carcinoma of the penis is rare with a reported rate of 1 person in 100,000 in developed countries. Circumcision is said to protect against this disease but this notion remains controversial (Boczko and Freed, 1979). Hypospadias, micropenis, Diphallia, or penile duplication are developmental disorders of penis considered rare condition do exist sometimes (Andrews et al., 1998).

**Scrotum:** The scrotum is a pouch-like structure that hangs behind the penis. It holds and protects the testes. It also contains numerous nerves and blood vessels. At lower temperatures, the Cremaster muscle contracts and pulls the scrotum closer to the body, while the Dartos muscle gives it a wrinkled appearance; when the temperature increases, the Cremaster and Dartos muscles relaxes to bring down the scrotum away from the body and remove the wrinkles respectively. The scrotum remains connected with the abdomen or pelvic cavity by the inguinal canal (Poncheietti et al., 2001).

**Testicular Anatomy:** The human testis is an ovoid mass that lies within the scrotum. The average testicular volume is 20 cc in healthy young men and decreases in elderly men (Crane and Scott, 2002). In Asian men, testes tend to be smaller. Normal longitudinal length of the testis is approximately 4.5 to 5.1 cm (Khan et al., 2010). The testicular parenchyma is surrounded by a capsule containing blood vessels, smooth muscle fibers and nerve fibers sensitive to pressure. The functional role of the testicular capsule is unknown, but may relate to movement of fluid out through the rete testis or control of blood flow to the testis (Crane and Scott, 2002). The testis contains seminiferous tubules and interstitial cells. The tubules are segregated into regions by connective tissue septa. The seminiferous tubules are long V-shaped
tubules, both ends of which usually terminate in the rete testis (Figure 2). Measurement of testicular size is critical in the evaluation of the infertile man, since seminiferous tubules (the spermatogenetic region of the testis) occupy approximately 80% of testicular volume. So, a rough estimate of spermatogenic cell capacity is provided by assessment of testicular size. Testicular consistency is also of value in determining fertility capacity. A soft testis is likely to reflect degenerating or shrunken spermatogenic components within the seminiferous tubules. The seminiferous tubules drain toward the central superior and posterior regions of the testis, the rete testis, which has a flat cuboidal epithelium. The rete coalesces in the superior portion of the testis, just anterior to the testicular vessels, to form 5-10 efferent ductules. These efferent ducts leave the testis and travel a short distance to enter the head, or caput region of the epididymis. The efferent ducts coalesce in a somewhat variable pattern within the caput epididymis to form a single epididymal tubule (Crane and Scott, 2002).

The artery to the testis is specialized in that it is highly coiled and intimately associated with a network of anastomotic veins that form the pampiniform plexus. The counter flowing vessels are separated only by the thickness of their vascular wall in some areas (Figure 2). This vascular arrangement facilitates the exchange of heat and small molecules, including testosterone (Wampler and Lianes, 2010). The transport of testosterone is a concentration-limited, passive diffusion process in men (Wampler and Lianes, 2010). The counter-current exchange of heat in the spermatic cord provides blood to the testis that is 2 to 4 °C lower than rectal temperature in the normal individual. A loss of the temperature differential is associated with testicular dysfunction in humans with idiopathic infertility, as well as men with varicocele or cryptorchidism.
Seminiferous Tubules

The seminiferous tubules provide a unique environment for the production of germ cells. The structures involved in this process include germinal elements and supporting cells (Mendez and Emery, 1979). The supporting cells include the peritubular cells of the basement membrane and the Sertoli cells. The germinal elements comprise a population of epithelial cells, including a slowly dividing primitive stem cell population, the rapidly proliferating spermatogonia, spermatocytes undergoing meiosis, and the metamorphosing spermatids (Mendez and Emery, 1979). The seminiferous tubule also produces an environment known as "the blood-testis barrier". The testis is unique in that the differentiating germ cells are potentially antigenic, and recognizable as foreign; however, little immunological reaction is usually detectable within the testis (Mendez and Emery, 1979).

Developmentally, the testis develops from the undifferentiated gonad. These primitive germ cells are referred to as gonocytes after the gonad differentiates into a testis by forming seminiferous cords. At this time, the gonocytes are located in a central position within the seminiferous cords. They are subsequently classified as spermatogonia after the gonocytes have migrated to the periphery of the tubule. From birth to approximately 7 years of life, there appears to be very little morphological change within the human testis. From 7 to 9 years of life, mitotic activity of gonocytes is detectable, with spermatogonia populating the base of the seminiferous tubule in numbers equal to those of the Sertoli cells (Mendez and Emery, 1979). There appears to be little further morphological change in spermatogonia until spermatogenesis begins at the time of puberty (Mendez and Emery, 1979).
**Epididymis:** The epididymis is a whitish mass of tightly coiled tubes cupped against the testicles, acts as a maturation and storage for sperm before they pass into the vas deferens, that carry sperm to the ampullary gland and prostatic ducts (Figure 3). The epididymis can be divided into three main regions: The head (Caput), the body (Corpus) and the tail (Cauda) (Jones, 1999) (Figure 4). However, these anatomical divisions have been defined based on findings in animals, not in humans. The human epididymal epithelium is relatively homogeneous as viewed under the microscope, and grossly, the epididymis does not have the same distinct gross anatomical subdivisions that are easily seen in the rat, rabbit and other animals. Unfortunately, there is little information available regarding the functional diversity of these three regions of the human epididymis (Jones, 1999). In reptiles, there is an additional canal between the testis and the head of the epididymis and which receives the various efferent ducts. This is, however, absent in all birds and mammals (Romer and Parsons, 1977).

Spermatozoa in the unobstructed testis are not motile and are incapable of fertilizing ova. Spermatozoa become functional gametes only after they migrate through the epididymis and undergo an additional maturation process, thereby acquiring the capacities for both progressive motility and fertility (Jones, 1999). Biochemical changes observed in human spermatozoa during epididymal transit involve the formation of disulfide bonds within the sperm nucleus and tail and the oxidation of sperm membrane sulphhydryl groups. These changes are thought to provide improved structural integrity to the sperm membrane. The changes in structural integrity of sperm may be necessary for the development of progressive motility and successful penetration of eggs. Pathology of epididymis includes an
inflammation of the epididymis is called epididymitis. It is much more common than testicular pain, called orchitis (Ross et al., 2011).

**Internal reproductive organs**

**Vas deferens:** The vas deferens, also known as the sperm duct, is a thin tube approximately 43.2 centimetres long that starts from the epididymis to the pelvic cavity. There are two ducts, connecting the left and right epididymis to the ejaculatory ducts in order to move sperm. Each tube is about 30 centimeters long (in humans) and is muscular (surrounded by smooth muscle) (Figure 5).

During ejaculation the smooth muscle in the walls of the vas deferens contracts reflexively, thus propelling the sperm forward. This is also known as peristalsis. The sperm is transferred from the vas deferens into the urethra, collecting secretions from the male accessory sex glands such as the seminal vesicles, prostate gland and the bulbourethral glands, which form the bulk of semen. The rate of transport of fluid through the vas deferens is not known in the human. Just prior to ejaculation, the testes are brought up close to the abdomen and fluid is rapidly transported through the vas deferens toward the region of the ejaculatory ducts and subsequently into the prostatic urethra. After ejaculation, intravasal fluid is transported back toward the epididymis and occasionally into the seminal vesicles as well (Kim et al., 2010). The retrograde transport of sperm to the seminal vesicles has been documented by videoradiography during ejaculation after vasography. The return of sperm to the seminal vesicles after ejaculation may help explain the prolonged presence of sperm in the ejaculate for some men after vasectomy. The vas deferens may be obstructed, or may be completely absent (the latter a potential feature of cystic fibrosis), causing male infertility. It can be overcome by Testicular Sperm
Extraction (TESE), collecting sperm cells directly from the testicles (Romer et al., 1977).

**Accessory glands**

Accessory glands are internal reproductive organs which provide fluids that lubricate the duct system and nourish the sperm cells. They are the seminal vesicles, the prostate gland, and the bulbourethral glands (Cowper glands) (Valerie, 2010)

**Seminal vesicles**

Seminal vesicles are sac-like structures attached to the vas deferens at one side of the bladder (Figure 6). They produce a sticky, yellowish fluid that contains fructose. This fluid provides sperm cells energy and aids in their motility.

About 50-70% of the seminal fluid in humans originates from the seminal vesicles, but is not expelled in the first ejaculate fractions which are dominated by spermatozoa and zinc-rich prostatic fluid (Kierszenbaum and Abraham 2002). The excretory duct of each seminal gland opens into the corresponding vas deferens as it enters the prostate gland. Seminal vesicle fluid is alkaline, resulting in human semen having a mildly alkaline pH. The alkalinity of semen helps to neutralize the acidity of the vaginal tract hence, prolonging the lifespan of the sperm. Acidic ejaculate (pH <7.2) may be associated with ejaculatory duct obstruction. The vesicle produces a substance that causes the semen to become sticky/jelly-like after ejaculation, which is thought to be useful in keeping the semen near the womb (Huggins et al., 1942).

**Prostate gland:** The prostate gland is responsible for the proof semen, a liquid mixture of sperm cells, prostate fluid and seminal fluid (Valerie, 2010). This gland is also responsible for making the semen milky in appearance by mixing calcium to the semen coming from seminal vesicle (semen coming from the seminal vesicle is
yellowish in colour); the semen remains cloudy and clumpy until the prostatic profibrinolysin is formed into fibrinolysin and lysis of the fibrinogen from the seminal vesicle fluids occurs (Myers and Robert 2000).

A healthy human prostate is classically said to be slightly larger than a walnut. The mean weight of the "normal" prostate in adult males is about 11 grams, usually ranging between 7 and 16 grams (Leissner and Tisell, 1979). It surrounds the urethra just below the urinary bladder and can be felt during a rectal exam. It is the only exocrine organ located in the midline in humans and similar animals (Figure 6). The secretory epithelium is mainly pseudostratified, comprising tall columnar cells and basal cells which are supported by a fibroelastic stroma containing randomly orientated smooth muscle bundles. The epithelium is highly variable and areas of low cuboidal or squamous epithelium are also present, with transitional epithelium in the distal regions of the longer ducts (Leissner and Tisell, 1979). Within the prostate, the urethra coming from the bladder is called the prostatic urethra and merges with the two ejaculatory ducts. The prostate can be divided in two ways: by zone, or by lobe. It does not have a capsule, rather an integral fibromuscular band surrounds it. It is sheathed in the muscles of the pelvic floor, which contract during the ejaculatory process (Raychaudhuri and Cahill, 2008).

**Bulbourethral glands**

The bulbourethral glands, also called Cowper glands, are two small glands located on the sides of the urethra just below the prostate gland. These glands produce a clear, slippery fluid that empties directly the urethra. They are homologous to Bartholin's glands in females (McEntee, 2012). The bulbourethral glands are compound tubulo-alveolar glands, each approximately the size of a pea in humans.
They are composed of several lobules held together by a fibrous covering. Each lobule consists of a number of acini, lined by columnar epithelial cells, opening into a duct that joins with the ducts of other lobules to form a single excretory duct. This duct is approximately 2.5 cm long and opens into the urethra at the base of the penis. The glands gradually diminish in size with advancing age (Schwartz, 1988).

During sexual arousal each gland produces a clear, salty, viscous secretion known as pre-ejaculate. This fluid helps to lubricate the urethra for spermatozoa to pass through, neutralizing traces of acidicurine in the urethra (Chughtai et al., 2005), and helps flush out any residual urine or foreign matter. Though the pre-ejaculate does not contain sperm it is possible for this fluid to pick up sperm, remaining in the urethral bulb from previous ejaculations, and carry them out prior to the next ejaculation. The Cowper's gland also produces some amount of prostate-specific antigen (PSA), and Cowper's tumors may increase PSA to a level that makes prostate cancer suspected (Chughtai et al., 2005).

**Role of Hormones in male reproduction**

Endocrine system is the second key regulator of organ system functions after nervous system in human body. Hormones are actual messengers in endocrine signaling. A man's sperm production is controlled via a complex interplay of hormones in the brain and the testicles. The control starts in the brain with the hypothalamus (under the brain) which releases Gonadotropin-releasing hormone (GnRH), a substance that promotes the pituitary gland to release two important hormones, Follicle stimulating hormone (FSH) and leutinizing hormone (LH). Follicle stimulating hormone travels in the blood to the testicles where it signals certain cells such as sertoli cells to produce sperm. When enough sperm is produced,
the testicular cells produce inhibin, a hormone that travels in the blood and gives signal to the pituitary gland to stop production and secretion of FSH. Leutinizing hormone also comes from the pituitary and travels to the testicles, where it signals to different cells, the Leydig cells to secrete testosterone (Heaton and Jeremy 2003). Testosterone is the male hormone but is not active reproductively until it is converted to dihydrotestosterone via an enzyme, 5-alpha-reductase. Dihydrotestosterone stimulates male reproductive tract growth and function. Testosterone and dihydrotestosterone inhibit pituitary production and secretion of LH when enough testosterone is synthesized (Mooradian et al., 1987).

Prolactin is a pituitary hormone that in men is not directly involved with reproduction. However, certain medical conditions can cause prolactin to increase, such as pituitary tumors, which in turn causes decreased production of FSH and LH by a variety of mechanisms. Estrogen, usually thought of as a female hormone, is present in men as well and is called estradiol. Estradiol levels are typically low, but may be elevated in certain conditions, such as obesity (Mooradian et al., 1987). Testosterone is converted to estradiol by an enzyme called aromatase. Aromataseis present in fat cells (Bassiletal., 2009).

By observing the levels of the various reproductive hormones, especially when analyzed in relation to a comprehensive history and physical examination, one can get a very good sense of a male's reproductive status as well as his prognosis for natural, biological fatherhood. In addition, there are hormonal conditions that can be treated with medical hormonal manipulation, often resulting in the patience's return to natural fertility. In addition, a comprehensive endocrine assessment will also detect potentially life-threatening medical conditions that are present in 2% of male fertility patients.
Diagnosis of male reproductive system through Ultrasonography

Medical imaging in infertile males

Technological advancement in the field of urology and imaging has led to enhanced diagnostic evaluation of the infertile male. Urological imaging and urology has coevolved replacing several invasive techniques like vasography, venography etc., that was previously employed (Anton and Mark, 2011). Several imaging techniques are available to evaluate men with obstructive infertility such as scrotal ultrasonography, transrectal ultrasonography (TRUS), vasography, Magnetic Resonance Imaging (MRI), TRUS guided seminal vesiculography etc. These advanced, highly specific imaging studies have enabled to identify specific abnormalities of physiological or anatomical significance which were previously ill defined, leading to selection of therapies designed to treat previously unmanageable post testicular abnormalities (Zahalsky and Nagler, 2001).

Obstruction of seminal tract

Post-testicular causes include obstruction of the sperm delivery route, anti-sperm antibodies and retrograde ejaculation. Obstruction can occur at any region of the seminal tract, either proximal, affecting the epididymis and scrotal portions of the vas deferens and distal which includes inguinal, pelvic and ampullary portions of the vas deferens, and ejaculatory ducts (Goluboff et al., 1995; Brugh and Lipshultz, 2007). Seminal tract obstruction may be congenital or acquired. Congenital causes include atresia (failure of normal opening) or stenosis (abnormal narrowing) as well as midline prostatic cystic lesions, e.g. utricular, Mullerian and ejaculatory duct cysts. Acquired causes may be of inflammatory or traumatic origin of the prostate, seminal vesicle or ejaculatory duct (Goluboff et al., 1995). Obstruction of the seminal tract is
observed to be the underlying cause among 6% of men complaining of fertility disorders (Schlegel, 2009).

I. Ultrasound Scanning

Ultrasound is cyclic sound pressure with a frequency greater than the upper limit of human hearing. The production of ultrasound is used in several fields including medicine, where the sound waves are directed to penetrate a tissue and measure the reflected signals called as echoes. This can reveal details about the structure of the tissue enabling to study any associated abnormalities.

Principle

The principle involves directing sound waves by means of a transducer (probe of appropriate length) to the area of interest. The waves interact with tissues of different density, absorptive and reflective characteristics (Honig, 1994). The piezoelectric crystals located in the probe transmit equal and opposite electric voltages that are transformed into ultrasound waves (Zhalsky and Nagler, 2001). Some of the transmitted sound waves are reflected back to the transducer which is transformed into electric potentials which are then converted to computer generated images (Honig, 1994).

Types

Ultrasound imaging techniques comprise real-time ultrasound, Doppler ultrasound, and Color Flow Doppler (CFD) imaging. Normal scrotal Ultrasound imaging employs a high resolution, ultrasound probe which is placed externally at the scrotum and movement in transverse as well as longitudinal plane a few millimeters provides real time images of the testis (Kim and Lipshultz, 1996). High frequency probe results in lower tissue penetration, high attenuation and better resolution. Real-
time ultrasound images are generated when high-speed ultrasonic beams create independent images at high rates, providing a dynamic image. This series of dynamic images may then be recorded in the form of a video or may be viewed as individual frames. For superficial examination of the scrotum and penis, a high-frequency probe (10 MHz) is optimal, providing greater resolution of the superficial areas of interest. A slightly lower frequency probe (6.5 - 7.5 MHz) permits deeper penetration, and is used for TRUS, where the ultrasound probe is placed within the rectum to view seminal vesicles, ejaculatory duct and prostate in real time (Honig, 1993).

Doppler ultrasonography enables to deduce the direction of blood flow. It is based on the pulsatile emission of ultrasound waves towards the moving target. The reflected tissue interface, i.e. blood, is moving, a frequency difference is created. This difference is converted into a visual signal which is then recorded electronically as a graph of frequency against time. A pulsed Doppler system measures the velocity of the moving tissue by the transmission at regular intervals of short bursts of ultrasound waves that are reflected from a moving tissue. Duplex Ultrasound combines pulsed Doppler with real time imaging and is extremely useful in imaging small blood vessels. Color flow Doppler ultrasonography also combines real time ultrasonography with pulsed Doppler and employs color identification of blood flow. Any alteration in the direction of blood flow is represented by a color reversal (Honig, 1993).

1. Scrotal Ultrasonography

Ultrasonography (US) is the primary imaging modality for assessing scrotal abnormalities (Kim and Lipshultz, 1996). Testicular abnormalities, which can be identified by means of ultrasonography include testicular tumors (benign and malignant) testicular cysts and testicular microlithiasis. The imaging is also used to calculate testicular volume and texture (Lenz et al., 1994). Testicular torsion can also
be accurately diagnosed when no blood flow to the testicle is demonstrated by CFD ultrasonography (Paltiel et al., 1998). Adnexal abnormalities, such as spermatoceles and hydroceles, are well visualized with scrotal ultrasonography, ruling out the need for further diagnostic exploration (Zahalsky and Nagler, 2001).

Other abnormalities that can be identified using US are varicoceles (pathological dilation of network of small veins draining the scrotum) and epididymal cysts. Scrotal US is of immense help in evaluation of azoospermic (semen devoid of sperms) subject as to whether the condition is due to obstruction or non obstruction as the imaging can detect abnormalities in testis, epididymis and the proximal vas deferens (Donkol, 2010).

### 1.1 Scrotal Ultrasonography in non obstructive Azoospermia and other infertile conditions

#### a) Size and texture

Scrotal US are employed to examine the size and echotexture in transverse as well as longitudinal plane. Testicular volume is positively correlated with the level of spermatogenic activity). The size has got profound influence on the sperm count as well as motility (WHO 2010). Lenz et al., (1994) employed a low frequency 7.5 millihertz transducer to measure the testicular volume (volume of ellipsoid). They demonstrated the mean volume of both the right and left testicles to be smaller when compared to the volume of normal men. In their study they were also able to identify a positive correlation between the volume and sperm count. The study also involved evaluation of the texture on a scale of 1 to 5 for increasing degree of irregularities. The asmedian score for the infertile group with regard to texture was observed to be 3 when compared to the median score of 2 observed in the normal men. This is
indicative of increased damage of seminiferous tubules in the testis of the infertile individuals.

**b) Testicular tumor**

Testicular tumors are observed to be more among infertile males when compared to normal individuals. The frequency of testicular tumors in infertile men was found to be 1 in 200 when compared to 1 in 20,000 among normal individuals (Zahalsky and Nagler, 2001). Testicular tumors cannot be appropriately detected by means of physical examination but can be made evident through color Doppler ultrasonography. In a review of ultrasonographic reports by Pierik *et al.*, (1999) it was identified that 60% of sonographic findings of abnormalities were not evident on palpation with only one in seven cases of tumors was suspected in physical examination.

**c) Testicular torsion**

Testicular torsion is a condition in which twisting of the spermatic cord results in progressive impairment of testicular venous drainage which ultimately leads to arterial ischemia and testicular infarction (Cuckow *et al.*, 2000). Testicular torsion is one of the leading causes of male infertility accompanied by acute scrotal pain. Torsion can lead to unilateral or bilateral anorchia, testicular atrophy, low sperm count, diminished motility and in severe cases may lead to azoospermia (Singh *et al.*, 2012). Persistent torsion can lead to ischemia and reperfusion injury which is associated with excessive production of Reactive Oxygen Species (ROS) leading to germ cell apoptosis, DNA damage, testicular atrophy and impaired spermatogenesis (Ichikawa *et al.*, 1993; Turner *et al.*, 1997). Testicular torsion can be identified by CFD
ultrasonography the observation being lack of blood flow to the testicle (Paltiel et al., 1998).

d) **Hydrocele**

Another abnormality that can be detected using scrotal ultrasonography is hydrocele which is an abnormal collection of fluid between the parietal and visceral layers of tunica vaginalis. Hydrocele is the most common cause of painless scrotal swelling (Rubeinstein et al., 2004). Primary hydrocele is usually of idiopathic etiology whereas secondary hydrocele can be caused by testicular torsion, infection, trauma, tumor etc (Singh et al., 2012). Mihmanli et al., (2004) observed that testicular size was larger in men with hydrocele which they propose is due to stasis in the venous and lymphatic outflow owing to pressure induced obstruction in the vessels of testis. They also observed that the testis returned to normal size after hydrocele excision.

The hydrostatic pressure of a hydrocele is more than the pressure in blood vessels within the scrotum. This affects the normal arterial blood flow which might result in an ischemic effect on the testis (Rados et al., 1996). Mihmanli et al., (2004) employed color Doppler ultrasonography to evaluate the blood flow before and after surgical removal of hydrocele and observed that the high-resistance flow in the intratesticular arteries prior to excision was substituted by a low-resistance flow after hydrocele excision which also resulted in the elimination of the high pressure. This altered blood pressure indicates that hydrocele has an ischemic effect on the testicular tissue ultimately leading to infertility.

e) **Epididymal cyst**

Epididymal cyst or spermatocoele are usually an associated finding but not contributing factor to infertility and are best detected by scrotal ultrasonography.
However, in certain conditions an epididymal cyst may become obstructive resulting in oligoasthenospermia or azoospermia condition. Chronic epididymal inflammation may lead to an enlarged, thickened epididymis with mixed echogenicity and calcification as a result of inflammatory response. Acute epididymitis may be confirmed from the findings of an enlarged epididymis with decreased echogenicity during an ultrasound scan (Kim et al., 1996).

f) Cryptorchidism

Cryptorchidism is the absence of one or both testicles from the scrotum due to failure of descend through the normal anatomical pathway (Lee et al., 1995). Cryptorchidism, whether congenital or acquired can lead to infertility by affecting the sperm concentration and sperm count. The extent of damage depends on several factors like testis location, temperature, hormone titre and associated structural anomalies. Semen analysis from men with untreated bilateral cryptorchidism reveals that the subjects were more inclined to be azoospermic and have higher rates of germ cell apoptosis than individuals with untreated unilateral cryptorchidism (Hadzisellimovic and Herzong., 2001; Chung and Brock, 2011). Moreover, 44–100% of men with treated bilateral cryptorchidism have been reported to have a low sperm count, low motility and abnormal morphology. Also more than 50% of the treated individuals were found to be azoospermic (Lee et al., 1995).

g) Varicocele

Varicocele is the pathological dilation of the pampiniform plexus of veins (network of many small veins draining the scrotum) of the spermatic cord (Agarwal et al., 2009). Several mechanisms have been demonstrated to be the pathophysiology of varicocele induced male infertility. These include hypoxia, testicular venous
hypertension, elevated testicular temperature, stasis etc. These effects the normal testicular function causing a decline in semen parameters like count, motility morphology etc. (Marmar et al., 2001). Clinical varicoceles are diagnosed by physical examination and confirmed by Ultrasound Color Doppler scanning which has better diagnostic accuracy than physical examination.

Scrotal US is highly reliable to diagnose varicocele and has been reported to have 97% sensitivity and 94% specificity (Trum et al., 1996). Real-time ultrasonography has also been used to diagnose the type of varicocele (grade I, II and III). Using high-frequency ultrasound (7 to 10 millihertz) probe, a varicocele is identified if there is dilation of the venous structures with the Valsalva maneuver (Mclure et al., 1991). Color flow Doppler ultrasonography has been demonstrated to have superior sensitivity and more noninvasive when compared to venography in diagnosing varicocele (Petros et al., 1991). Employing CFD the characteristic alteration in the direction of blood flow in varicocele condition can be identified by the color reversal (red to blue or blue to red) (Zahalsky and Nagler, 2001).

1.2 Scrotal Ultrasonography in obstructive Azoospermia and other infertile conditions

Evaluation of the epididymis and testicular volume with scrotal US are vital for distinguishing obstructive azoospermia from non-obstructive azoospermia among infertile men. Testicular volume measured by scrotal US is higher for obstructive azoospermia than for nonobstructive azoospermia. A study conducted by Moon et al., (2006) revealed that the median testicular volume in obstructive azoospermia was 11.6 mL (range, 7.7-25.8 mL) and that in nonobstructive azoospermia was 8.3 mL (range, 1.2-16.4 mL). Scrotal US are employed to detect abnormalities in the proximal portion of the seminal tract by demonstrating dialation in the proximal seminal duct
(mediastinum testis, epididymis, and intrascrotal portion of the vas deferens) and can also provide insight into secondary changes of the proximal seminal duct caused by obstruction in the distal part of the seminal duct (terminal vas deferens, ampulla of the vas deferens, seminal vesicle, and ejaculatory duct) (Beddy et al., 2005). The epididymal abnormalities depicted with scrotal US are significantly associated with obstructive azoospermia. Sensitivity, specificity, and accuracy of scrotal US for differentiation of obstructive from nonobstructive azoospermia were found to be 82.1%, 100% and 87.5% respectively (Moon et al., 2006).

II Transrectal Ultrasonography

Transrectal Ultrasonography is most commonly performed if the diagnosis of distal seminal tract obstruction associated with vassal ampullae, seminal vesicles and ejaculatory ducts and is widely used in the diagnosis of distal genital ductal system abnormalities (Galuboff et al., 1995; Kim et al., 1996). Prior to the advent of TRUS, the seminal vesicles and ejaculatory ducts were imaged by vasography which is associated with risk of vassal scarring and subsequent obstruction (Honig, 1993). Recent improvements in TRUS with the use of higher frequency multiplanar transducers have enabled the ejaculatory ducts to be visualized and imaged more frequently than in the past (Clements et al., 1991). TRUS findings that affect infertility consistant with Ejaculatory duct obstruction (EDO) include ejaculatory duct calcifications, ejaculatory duct cysts, and dilated ejaculatory ducts or seminal vesicles. The primary use of TRUS is to assess obstructions and to determine the absence or hypoplasia of the seminal vesicle and ejaculatory ducts. TRUS has been combined with seminal vesiculography to search for distal ejaculatory duct obstruction, thereby greatly reducing the need for the more invasive open vasography. Currently, the most important indication for TRUS to assess for obstruction, the absence or hypoplasia of
the seminal vesicles and the ejaculatory ducts, is low ejaculate volume, azoospermia, severe oligospermia and asthenospermia (Zahalsky and Nagler, 2001).

The advantage of TRUS is that it is non-invasive, low cost, wider availability and assists in visualizing the normal and abnormal seminal vesicles, the vasa deferentia, ejaculatory ducts and the prostate. Absolute indications for performing TRUS include low volume azoospermia in the absence of testicular atrophy and low volume severe oligoasthenospermia, when (for both) retrograde ejaculation is not present. When an ejaculatory duct obstruction is suspected, TRUS is now considered the initial diagnostic modality (Kim and Lipshultz, 1996).

a) Ejaculatory duct obstruction

Ejaculatory duct obstruction is a correctable cause of male infertility and is now considered to affecting 1–5% of infertile men and can be due to either acquired or congenital causes (Engin et al., 2000; Purohit et al., 2004). The acquired causes include trauma, inflammation, calculus formation and infection while congenital abnormalities include atresia, stenosis, cysts (Muellerian, utricular and wolffian) and genetic abnormalities as well as Mullerian, utricular and Wolffian cysts (Singh et al., 2012). Ejaculatory obstruction primarily leads to infertile condition while other symptoms include decreased ejaculate force, pain during ejaculation, hematospermia, perineal or testicular pain, prostatitis-like symptoms etc (Galuboff et al., 1995). Physical examination of individuals with EDO reveals normal testis, vas deferens and secondary sexual development (McIntyre and Fish, 2010), while semen analysis records low-volume, azoospermia or oligozoospermia, negative or very low fructose content, and low or immotile sperms (Philip et al., 2007) When the diagnosis is complete EDO, TRUS guided aspiration of dilated or cystic ejaculatory ducts or seminal vesicles is undertaken to look for presence of sperm. If sperms are observed,
then surgical endoscopic relief of the obstruction by transurethral resection of ejaculatory ducts (TURED) is performed which restores communication between ejaculatory duct and urethra (Heshmath and Lo, 2006). When the aspirate is devoid of sperms than vasotomy or vasography are performed to visualize the anatomy of the seminal vesicles, ejaculatory ducts and distal vasa deferentia to exactly demarcate the site of obstruction as well as to identify any associated atresia or stenosis in the distal vas deferens. This is followed by microsurgical epididymal sperm aspiration without EDO repair. If sperm are identified in the vasal aspirate, endoscopic relief of EDO is generally performed. In the absence of vasal sperm, (Shabsigh et al., 1989; Kim and Lipshultz, 1996).

b) Congenital absence of Vas deferens

The vas deferens is a paired tubular structure that extends from the caudal region of the epididymis into base of the bladder through the inguinal canal. At the internal ring, the vasa deferentia curve laterally and then pass medially downward into the pelvis where they join the seminal vesicles to form ejaculatory ducts. The human vasa deferentia have a total capacity of 0.45 ml, which accounts for roughly 10% of the volume of normal ejaculate (Singh et al., 2012). Congenital absence of the vas deferens (CBVAD) is diagnosed in 1.3% of men who are subjected for fertility evaluation of which 4.4–17.0% of men record azoospermic condition and 25% of men record obstructive azoospermia (Jequier et al., 1985; Goldstein and Schlossberg, 1988; Futterre et al., 2008).

Vasal agenesis can be partial or complete, unilateral or bilateral, and in few cases found to be associated with epididymal hypoplasia. Infertile individuals with CBAVD display a spectrum of abnormalities including preserved caput epididymis, and absence or abnormal seminal vesicles (Oates and Amos, 1993). The testis is
usually found to be normal in both size and function among these individuals. They are observed to be azoospermic with low semen volume (<1 ml), low levels of fructose (seminal vesicular origin), α-glucosidase (epididymal origin) and more acidic (Oates and Amos, 1993).

Among men complaining of fertility disorder an approximate 1% of men have unilateral vasal agenesis and these men are usually fertile owing to single vas deferens. However they are more prone to become infertile than the general population as they have a single functioning testis. It is observed that 20% of affected men have aplasia of the contralateral seminal vesicle and atresia of the ampullary portion of the contralateral vas deferens. Hence a subset of men with unilateral vasal agenesis has azoospermia or other abnormal semen parameters (Hall and Oates, 1993). TRUS is employed to evaluate the ampullary portion of the contralateral vas deferens and the seminal vesicles. Obstructive azoospermia in these individuals is treated by testicular or epididymal sperm retrieval techniques followed by In vitro Fertilization (IVF) or IntraCytoplasmic Sperm Injection (ICSI).

c) Abnormalities associated with Seminal Vesicles

The seminal vesicles are paired, symmetric, saccular, elongated organs which lie cephalad to the prostate and posterior to the bladder. They are best visualised through TRUS by means of transverse imaging. The vasal ampullae are best visualized in transverse section just medial to the seminal vesicles (Kim and Liphultz, 1996). The seminal vesicles serve as reservoirs of seminal fluid but no significant change in volume has been demonstrated after ejaculation. Ejaculatory duct obstruction is often associated with seminal vesicle dilation but is not found in every individual. However asymmetry in the pair is an indication for ejaculatory duct obstruction. Almost 90% of infertile individuals with unilateral CAVD might have
aplasia of the ipsilateral seminal vesicle, and close to 20% of these individuals might have aplasia of the contralateral seminal vesicle. All these abnormalities can be identified and characterised by means of TRUS. In those men with CBAVD, 16% had bilateral aplasia of the seminal vesicles, whereas 21% had unilateral seminal vesicle aplasia and contralateral seminal vesicle hypoplasia. Hypoplasia has been defined as a decrease in normal size of 30% (Kim and Liphultz, 1996).

TRUS-guided seminal vesiculography is a technique that combines Ultrasonography with radiography to evaluate seminal vesicle abnormality. Seminal vesiculography is performed by means of fine needle puncture of the seminal vesicle to inject contrast material for radiography. Seminal vesiculography has helped imaging of the distal male reproductive tract (vas deferens, seminal vesicles, and ejaculatory ducts). Real-time TRUS visualization has also been used to guide aspiration of seminal vesicles to diagnose EDO. The presence of sperm in the aspirated fluid confirms the presence of obstruction (anatomical or functional) as well as rules out more proximal obstruction. It also confirms the presence of normal spermatogenesis. The presence of more than three motile sperm per high-power field in the seminal vesicle aspirate is considered as an indication of obstruction (Jarow, 2001).

Fine needle aspiration of abnormally dilated cysts, seminal vesicles, or ejaculatory ducts is performed through guidance by means of TRUS. The aspiration of cystic structures can also be performed and the fluid can be evaluated for the presence of sperm. A contrast material is then injected into the punctured structure and then plain radiographs are taken. The “vesiculogram” films then are reviewed for the presence of dilated seminal vesicles, EDO, or other correctable anatomic abnormalities that may be causing infertility (Zahalsky and Nagler, 2001).
d) Cystic lesions of the Prostate

Imaging techniques such as TRUS and endorectal MRI has improved the detection of cystic lesions of the prostate (congenital or acquired), which affects 0.5–7.9% of men. Two types of cyst, namely midline prostatic cysts and ejaculatory duct cysts can obstruct the ejaculatory ducts and lead to infertile condition (Hamper et al., 1990). Midline prostatic cysts can be divided into three types: prostatic utricle cysts (previously called Mullerian duct cysts), cystic dilatation of the prostatic utricle and enlarged prostatic utricles (Galosi et al., 2009). A prostatic utricle cyst results from failure of the Mullerian ducts to regress and affects 5% of men with obstructive azoospermia. Prostatic utricle cysts do not communicate with the urethra and hence aspirations from these cysts do not contain spermatozoa (Singh et al., 2012; Kato et al., 2002). The condition is usually asymptomatic, but patients in the third or fourth decade of life may develop irritative and obstructive urinary symptoms as well as hematuria, hematospermia, bloody urethral discharge, ejaculatory pain, urinary tract infection, epididymitis, infertility and constipation.

Cystic dilation of the prostatic utricle (cystic utricle) arises due to obstruction of the junction between the utricle and the urethra hence communicates with the posterior urethra. These cysts are smaller than prostatic utricle cysts and are localized to the midline. Both prostatic utricle cysts and cystic utricles can enlarge and compress both ejaculatory ducts resulting in abnormal semen parameters and might also cause azoospermia (Kato et al., 2002; Kato et al., 2005).

The third type of midline prostatic cyst is an enlarged or hypertrophied prostatic utricle that communicates with the prostatic urethra and is frequently found in children with urogenital malformations, such as proximal hypospadias or virilization defects. TRUS and cystourethrography usually reveal an enlarged prostatic
utricle that is midline and posterior. This type of cyst does not typically obstruct the ejaculatory ducts.

e) Ejaculatory duct cysts

The ejaculatory duct is formed by the confluence of the seminal vesicle and the terminal ampullary portion of the vas deferens. The ampulla of the vas deferens can be imaged in both the transverse and sagittal planes. They appear as a pair of oval, convoluted, tubular structures medial to the seminal vesicles and cephalad to the prostate (Kim and Liphultz, 1996). Ejaculatory duct cysts (congenital or acquired) originate from the Wolffian ducts and occupy a paramedian or median position in the prostatic gland above the level of the verumontanum. They can be unilateral or bilateral and etiologies include partial distal obstruction caused by chronic infection, transurethral manipulation, tuberculosis or urethral foreign body and are commonly associated with obstructive azoospermia. Small cysts appear as intra-prostatic masses lateral to the midline at the base and midline at the level of the verumontanum during TRUS. If the cysts are large these lesions resemble cystic utricle and prostatic utricle cysts. Small cysts are usually asymptomatic while large ones can cause hematospermia, ejaculatory pain, azoospermia and male infertility.

The condition is diagnosed by TRUS and ultrasonography guided transperineal aspiration of cystic fluid is employed to detect the presence of sperm. Small and asymptomatic cysts do not require treatment but cysts that cause hematospermia, low semen volume, abnormal semen parameters, infertility and infections must be treated. Treatment modalities include simple transrectal aspiration, sclerotherapy of the cyst under TRUS guidance, open surgical removal, and TURED. These treatments usually result in appearance of sperm in the ejaculate and restores fertility.
Significance of Transrectal Ultrasonography in management of male infertility

- Evaluation of size, shape and position of Vas deferens, seminal vesicles prostate and their anatomical and pathological changes

- Early diagnosis of carcinoma of the prostate (CAP) based on biopsy results along with abnormal digital rectal examination findings, elevated prostate-specific antigen (PSA) levels, or both (Ultrasonographic findings alone cannot be used to establish or exclude the diagnosis of CAP.)

- Evaluation of men with azoospermia to rule out ejaculatory-duct cysts, seminal vesicular cysts, müllerian cysts, or utricular cysts

Infertile men with primary testicular failure can proceed directly to an advanced assisted reproductive technique such as intracytoplasmic sperm injection or IVF. On the other hand infertile condition arising due to obstructions of the seminal tract may be amenable through surgical or interventional correction. This has enabled to devise systemic simpler therapies instead of prematurely restoring to Assisted Reproductive Techniques. The rapid progress in diagnostic options employing Ultrasonography and TRUS combined with improvements in the treatment modalities has allowed physicians to treat the infertile male successfully. In case of assessment of infertile individuals, the enhanced ultrasound resolution provided by high-frequency transducers has enabled better resolution with reference to the number of pathologic processes that may be observed within the testes, paratesticular structures, genital ducts, and accessory reproductive organs. Abnormalities that were rarely identified have become easily visible resulting in more precise and appropriate treatment for male infertility.

The present investigation is maiden report in south India in which an attempt has been made to study the male infertility systematically in relation to anatomical and pathological changes in the reproductive organs in Mysore.
Objectives:

1. To carry out physical examination of the subjects with reference to reproductive organs including per rectal examination of the internal genital organs.

2. To establish the spermiogram and to carry out hematological analysis through physical and chemical parameters.

3. To investigate the reproductive hormones such as Testosterone, Estrogen, Luteinizing hormone (LH), Follicle stimulating hormone (FSH), and Prolactin for the subjects.

4. To investigate the external genital organs through Ultrasound scanning by color doppler for testis and epididymis and Trans Rectal Ultrasound Scanning (TRUS) for internal reproductive organs among infertile males.