Review of Literature
One of the earliest studies on the epidemiology of infertility is that of Duncan, J.M (1866) who attempted to evaluate the aetiology of infertility using the conventional methods promulgated by WHO for the study of semen quality and sperm function testing. However these are of limited diagnostic value at present because, a number of general epidemiological factors are known to have influence in a couple's fertility. For example, age, smoking habit, occupational, environmental and genetic factors are highly relevant in determining the fertility of an individual.

I. ENVIRONMENTAL FACTORS

Cigarette smoke

The studies made by Sofikitis et al., (1995) almost conclusively found out that cigarette smoking can cause sub-fertility in males and might result in decreased sperm concentration, low sperm motility and reduced percentage of morphologically normal sperms. The studies were made by Vine (1996) on the relationship between cigarette smoking and semen quality. Close et al. (1990) had reported a significant elevation of round cells and leucocytes in the ejaculate of smokers when compared with those of non smokers. Sharma and Agarwal (1996) suggests the leucocytes to
be the major sources of reactive oxygen species (ROS) in the ejaculate. Ochsendrof (1999) suggested that higher levels of leucocytes might impair male fertility by formation of ROS. Zavos et al. (1998) compared the semen quality of smokers and non-smokers and found that the spermatozoa count of smokers was much lower and low motility is associated with structural abnormalities of the sperm tail. The most severe abnormality noted was the disappearance of one or more of the nine fiber-doublets and one or more of the central fibers.

**Alcohol**

Anderson et al (1983) reported the use of alcohol in men was associated with testicular atrophy. Additionally, no clear association between paternal alcohol exposure and subfecundity had been detected by Olsen et al (1997) and Jensen et al (1998).

**Occupational Exposures**

**Heat exposure**

Mieusset and Bujan (1995) indicated testicular heating as a factor contributing to male sterility. They have observed that, increased testicular temperature was generally seen associated with abnormalities such as cryptorchidism, retractile testis, varicocele and acute febrile illness. Thonneau, et al. (1996) reported a gradual decline in sperm production in people with certain life style such as
remaining in a sitting posture in a vehicle for prolonged periods. They found that the time taken by couples to conceive was significantly longer for couples in which the man was seated for more than three hours per day for occupational reasons, than for other couples. The study made by Figa Talmanica et al. (1996) among the taxi drivers of Italy also showed that the percentage of spermatozoa with normal morphology was significantly lower in taxi drivers than the controls.

Brindley (1982) observed that in paraplegic men moving in wheel chairs maintain a scrotal temperature about 0.9°C higher than the normal. He further observed a significant correlation between the deep scrotal temperature of >36.3°C and low motile sperm counts in paraplegic men. The studies made by Bonde (1992) on the semen quality of 17 welders who were exposed to radiant heat did not find any significant fall in the sperm count. However, the proportion of spermatozoa with normal shape declined significantly after six weeks of heat exposure and increased after a break in exposure to heat.

Tas et al. (1996) made a detailed study of the occupational hazards in workers associated with rubber, petroleum, agriculture, chemicals, printing and welding and observed detrimental effect of these on male reproductive systems of these workers. Schrader
and Turner (1988) while studying the effect of ethylene dibromide on occupational exposure found its adverse effects on sex glands affecting sperm viability and sperm motility. In order to make an assessment of the endocrine dysfunction they have suggested evaluation of the hormone levels of FSH, LH, testosterone and prolactin in blood and urine. Schrader (1988) also suggested the effects of toxicants on the male reproductive system at one of several sites such as testis, accessory sex glands comprising epididymis, prostate and seminal vesicles as well as the neuroendocrine system.

**Organic solvents**

Veulemans et al. (1993) has shown the effect of exposure to ethylene glycol ethers in causing spermatogenic disorders. Schrader and Turner (1988) while studying the effect of ethylene dibromide on occupational exposure found its adverse effect on sex glands affecting sperm viability and sperm motility. Schrader et al., (1988) made a comparative study of the effects of short term and long term exposure of ethylene dibromide on the accessory sex glands in humans especially on semen volume and motility of the sperms. It was observed that chronic exposure decreased sperm motility and viability, decreased seminal fructose level and increased semen pH. The presence of EDB metabolites was also observed in
the semen of workers who were exposed to this toxicant. Other potential toxicants found to be present in the semen were lead, cadmium, hexachlorobenzene, hexachlorocyclohexane, dieldrin and polychlorinated biphenyls.

**Heavy metals**

Stachel et al. (1989) detected the presence of heavy metals in the seminal plasma using absorption photometry. Coste et al. (1991) have suggested the role of heavy metals like cadmium, lead, arsenic and zinc in impairing spermatogenesis.

**Environmental contaminants**

Anderson et al. (2000) have observed that there has been considerable deterioration in the human male reproductive function during the last 4-5 decades. Their observations were based on the evidences from the literature and on the number of couples seeking fertility treatment because of poor semen quality in people especially of industrialized countries. Carlsen et al. (1992) observed a significant decline in the mean sperm concentration from $113 \times 10^6$/ml in 1940 to $66 \times 10^6$/ml in 1990. Similar observations were also made by Auger et al. (1995), Irvine et al. (1996), Van Waelegham et al. (1996) and Swan et al. (1997). An increase in the incidence of other reproductive diseases / abnormalities such as testicular cancer, hypospadius and cryptorchidism have also been
observed by Adami et al. (1994) and Moller et al. (1996). The exact reasons for these abnormalities are not known although Skakkebaek et al. (1998) attempted to correlate the germ cell cancer and disorders of spermatogenesis with environmental factors. Possible causes of this alleged decline including the estrogenic activity of several environmental pollutants, have been the subject of extensive discussion [Sharpe and Skakkebaek, 1993; Jesen et al., 1995; Safe 1991; Toppari et al., 1996; Cooper and Kavlock 1997; Daston et al., 1997]. The environmental oestrogen might affect the development of the male reproductive system during foetal or childhood life [Sharpe and Skakkebaek, 1993; Jensen et al., 1995; Cooper and Kavlock, 1997]. But from studies on occupational exposure to high amount of chemicals, it is known that spermatogenesis can also be corrupted by exposure of the adult man to various organic chemicals [Whorton et al., 1977; Emmett et al., 1988; Tas et al., 1996; De Celis et al., 2000]. Suspect agents of endocrine disrupting activity, possibly interfering with male reproductive capacity, are chlorinated hydrocarbons, for instance polychlorinated biphenyls (PCB) and pesticides. In vivo formed PCD metabolites, especially hydroxy-PCB, might play an even more important role. In in–vitro studies, such metabolites have been shown to exhibit a much stronger estrogenic activity than the
unmetabolized compounds [Korach et al., 1988; Waller et al., 1995]. Furthermore, anti-androgen activity Kelce et al. (1995) and anti estrogen activity might also be involved in the disturbance of the delicate hormonal balance that regulates spermatogenesis Cornor et al. (1997). Navas and Segner, (1998).

The effects of environmental and occupational aspects on sperm motility were studied by Fisher-Fischbein (1990) who suggested impairment of reproductive capacity in men who are exposed to environmental and occupational toxic agents. Many chemical agents are known to affect male reproduction by direct effect and by their mutagenic effect. The mechanism involves hormonal control of spermatogenesis or directly affecting germ cells and sertoli cells of the testis. (Sofikitis et al., 1995).

Kogevinas (2001) suggested that the chemicals of the environment especially those that mimic or block endogenous hormones might disturb the delicate balance maintained by endocrine system. An increase in the incidence of testicular cancer, cryptorchidism, hypospadius and decline in the sperm count are attributed to the presence of the above mentioned chemicals of the environment. Skakkebaek et al. (2001) suggested that increasing incidence of reproductive abnormalities might be related to oestrogen exposure disrupting the development of testes and male
reproductive tract. Weber et al. (2002) gives a list of chemicals that affect the human reproductive system through endocrine mechanisms. The list includes pesticides, polychlorinated biphenyls, dioxins, phytoestrogens and mycotoxins.

Although male reproductive toxicology had been an area of interest for the last several decades, it was the study of Whorton et al. (1977) established the role of toxicants in male infertility. As early as 1961, animal toxicologists reported that DBCP an important component of the pesticides, reduced the testicular weight in animals exposed to these chemicals. This work remained unnoticed until Whorton et al. (1977) reported the effect of DBCP causing male sterility in humans. Since then, several other chemicals have been identified having adverse effect on male fertility. Whorton et al. (1979) observed that exposure to DBCP reduced sperm counts to 46 million per ml from 79 million per ml of unexposed men. Ratcliff et al. (1987) observed that long term exposure to ethylene dibromide (EDB) increased the number of sperms with tapered heads and decreased the total number of sperms per ejaculate. Lerda and Rizzi (1991) observed that male persons occupationally exposed to 2,4-dichloro phenoxy acetic acid (2,4D) suffered from reproductive dysfunction associated with asthenozoospermia, necrozoospermia and teratozoospermia. They also observed a lower sperm
concentration and an increase in the tapering head defects in the agricultural workers who were exposed to these chemicals.

II. IATROGENIC FACTORS

Medical or surgical intervention for the treatment of disease care also cause male sterility in certain cases. Hotchkiss (1970) initially reported that some male infertility patients had either unilateral or bilateral occlusion of the vas deferens following childhood inguinal herniorrhaphy. They concluded that the incidence of ASA after childhood inguinal herniorrhaphy was similar to the incidence of ASA vasectomy patients.

III. ACQUIRED DEFECTS OF THE TESTIS, PROSTATE OR SPERM

Diehl and Hondl (1990) observed varying degrees of permanent damage to the seminiferous tubules when puberlator adult testes were involved in mumps orchitis. Niermann (1980) reported that male infertility could occur after mumps infection without mumps orchitis. Some investigations accepted that one factor that could negatively affect fertility after mumps orchitis is the humoral immunity against spermatozoa – the sperm antibodies. (Hafez, 1976; Tung and Menge 1985; Shulman, 1995). Prevenden et al. (1996) also observed a significantly low percentage of sperms with normal morphology in men with a past history of mumps.
The relationship between sexually transmitted diseases and male infertility was studied by Moskowitz, et al (1992). Their studies revealed that men with past history of STD had significantly lower measures of semen volume (about 1.6 ml) when compared with that of men who had no past history of STD (2.4 ml). An increase in the number of WBC in the semen is found to be generally associated with bacterial infections. Berger et al. (1983) noted a reduction in the seminal WBC after antibiotic treatment of patients with potential pathogenic such as ureoplasma, urealyticum and Chlamydia trachomatis.

Aitken et al. (1989) proposed generation of reactive oxygen species that could lead to peroxidative damage of the sperm membrane fluidity. Formation of autoantibodies against one's own spermatozoa associated with certain diseases such as urethritis, prostatitis and epididymitis was reported by Aitken (1989) and Jarow (1990). Bar-Chama and Fish (1993) indicated that acute and chronic infection of the genital tract might play an important role in male factor infertility due to deterioration of the spermatogonia, impairment of sperm function and obstruction of seminal tract. Weidner (1990) also observed that in nearly 60% of the patients with acute epididimitis, spermatogenesis was found to be impaired.
Jarow et al. (1990) observed antisperm antibodies in the blood serum and seminal plasma in person suffering from chronic prostatitis. Chlamydial infection leading to tubal infertility of his partner and seminal leucocytosis are also known to cause sterility (Westron, 1996). Male sterility is also seen directly or indirectly associated with many general medical disorders like diabetes and hypertension (Irvine, 1998).

**Antisperm antibody**

Antisperm antibodies research began in 1899 when Landsteiner initially reported that sperm could be antigenic if injected into a foreign species. After this, Metalnikoff (1974) found that sperms were also antigenic when injected into the same species. Alexander et al. (1979) and Mandelbaum et al. (1987) reported that mechanical obstruction of the genital tract might occur as a result of congenital anomaly, vasectomy or trauma. Gilbert et al. (1989) demonstrated the presence of sperm bound immunoglobulins in 32% of infertile men with palpable varicocele. They also noted that men with sperm bound immunoglobulins demonstrated significant decreases in sperm concentration and motility as well as an increase in abnormal morphology. Kortebani et al. (1992) examined leucocyte populations in semen samples.
from 279 infertile men and concluded that inflammation might lead potentially to genital tract disruption and ASA formation.

**Varicocele**

The role of varicocele influencing male infertility was first noticed by Tulloch (1952) who reported the beneficial effects of varicocele treatment in improving male fertility. Ali et al. (1990) could correlate the influence of scrotal temperature and semen quality in people with varicocele. Several studies have been made to know the effect of varicoceles and abnormal dilation of the testicular veins on semen quality and infertility. Rodriguez et al. (1981) made a comparative study of the sperm morphology of 56 men with varicocele and 126 men without varicocele and found no significant differences in infertility. However, Naftulin et al. (1991) observed a poor semen quality in persons suffering from varicocele. The sperm parameters showed a decrease in the number and motility of the sperms and an increase in the occurrence of sperm head abnormalities. A comparative study of the hormonal patterns made by Hanns et al. (1991) in persons with and without varicocele suggested normal hormonal values for both, although Castro-Magana et al. (1990) noticed a correlation between the impairment of spermatogenesis and Leydig cell function. Gorelick and Goldstein (1993) observed that nearly 80% of the people suffering from
varicocele had secondary subfertility and suggested that this might be due to progressive testicular damage occurring in those persons associated with increased scrotal temperature, venous stasis, reduced oxygen tension and accumulation of toxic metabolites. Gorelick and Goldstein (1993), however, suggested that varicocele could be treated by surgical or non surgical methods. Benoff et al (1997) proposed that the defects of sperm structure observed in the varicocele patients might be due to their excessive cadmium exposes.

**IV. DEVELOPMENTAL AND STRUCTURAL DEFECTS OF THE TESTIS OR SPERM**

*Genetic Causes*

Chandley et al. (1986) in their studies associated male infertility to structural defects on the Y chromosome such as deletion, of the distal fluorescent heterochromatin region of the long arm. Zuffardi and Tiepolo (1982) while studying the frequencies and types of chromosome abnormalities associated with human male infertility have observed that the structural chromosomal abnormalities were ten times more frequent in infertile males than in normal males. Giorlandino et al. (1998) observed that increased frequencies of chromosomal aberrations result in higher rate of recurrent abortion. Lilford et al. (1994) attempted to study whether oligoasthenoteratospermia has any familial component or not.
However, they could not characterize the sperm abnormalities or explain the genetic mechanism of transmission. One of the early studies on the role of chromosomal abnormalities in male fertility is that of the presence of Barr body in out of the 91 males studied for azoospermia or severe oligospermia Ferguson Smith et al. (1957). Jacobs and Strong (1959) observed the presence of XXY chromosomes in these individuals who were Klinefelter syndrome. Chandley (1979), while studying the chromosomal basis of human infertility observed that nearly 20% of the idiopathic males were due to male factor subfertility involving trisomy of sex chromosomes. Dela chapelle et al. (1990) while studying the etiology of the sex reversed observed 373 individuals with 47, XXY karyotype in a sample of 10728 men whose karyotypes were studied. This was the most frequently detected karyotypic abnormality. Mosaics of 46,XY and 47,XXY were also found to be relatively common especially in azoospermic and severe oligospermic males. Jacobs and Hassold (1995) suggested that most numerical chromosomal abnormalities originate at mitosis while structural abnormalities might have de nova origin. Giorlandino (1998) observed that the chromosomal abnormalities occurring in spermatozoa might cause higher rate of recurrent abortion. Nicolaidis (1998) suggested that the most numerical and autosomal anomalies originate during maternal
mitosis although some are of paternal origin. Chandley (1979) observed the frequency of chromosomal aberrations ranging from 2.2% in subfertile males to 6.0% in oligospermic males and 15% in azoospermic males. The incidence of Klinefelter syndromes (47,XXY) in patients with male factor subfertility was found to be 5 to 7% and they were usually infertile. Jequier et al. (1985) reported congenital bilateral absence of vas deferens (CBAVD) in about 1% of infertile patients. They demonstrated that CBAVD is strongly associated with mutations and splice variants in the cystic fibrosis transmembrane regulator gene (CFTR gene) on chromosome 7. Okada et al. (1999) and Meng et al. (2001) also observed impairment of spermatogenesis in men with congenital absence of vas deferens.

A karyotypic survey conducted by Chandley (1979) among 6982 subfertile males indicated higher percentage of chromosomal anomalies when compared with that of general population. Bhasin (2000) observed that sex chromosomal anomalies in infertile men were 15 times more than in the general population. Similarly, autosomal abnormalities were six times greater than in general population. Among these, Klinefelter syndrome was found to be about one in 500. Bielanska et al. (2000) also observed that in 93% of cases the syndrome possessed the characteristic
Karyotypes 47,XXY while variants such as 47,XXY, 46,XY and mosaics with 48,XXYY, 48,XXXY and 49,XXXY abnormalities were also present in their studies. Krausz and Forti (2000), while studying the clinical aspect of male infertility observed several structural abnormalities of chromosome including reciprocal translocation Robertsonian translocation, paracentric inversions and marker chromosomes. They also reported that the frequency of autosomal translocation in infertile men was about 7 times more in infertile men when compared with general population. De Braekeler and Dao (1991) had also noticed the frequency of marker chromosome 8 times more in infertile men. Among these anomalies Robertsonian translocation were found to be prevalent in oligozoospermic males but rare in azoospermic patients. Moosani et al. (1995) and Hassold et al. (1996) have established that men with idiopathic oligozoospermia or azoospermia have higher risk of carrying constitutional chromosomal abnormalities than fertile males. Martin (1995) indicated that in patients with normal karyotype, the incidence of spermatozoal aneuploidies was increased on account of alterations occurring during chromosome segregated process. Hassold et al. (1996) have also reported that morphological abnormalities in sperm heads are associated with defects in their chromosome content. In'tVeld (1997) described a case of unusual
spermatozoal morphology with large sperm head and multiple tails associated with polyploid condition. Escalier et al. (1993) have suggested that macrocephalic spermatozoa could appear due to failure in mitotic division, disturbance of the sperm centrioles or due to defective cytokinesis. Escalier (1999) further showed that tetraploid spermatozoa called large heads, could differentiate into spermatids in spite of mitotic alterations. It was further observed that the patients with macrocephalic spermatozoa apparently related with spermatogenic arrest at the mitotic stage. Egozcue (1989) while studying the chromosomal aspects of male infertility observed that somatic chromosome abnormalities were 10 times more in infertile men than in general population Retif (1986) also observed high frequency of numerical and structural anomalies especially in azoospermic and severely oligoasthenospermic men. Vendrell et al. (1999) observed low motile sperm concentration, moderately hypoplastic testicular volume, slightly elevated baseline serum FSH level and low count of mature spermatids per tubule in patients suffering from severe nonobstructive oligoasthenozoospermia. They also noted 37.9% mitotic abnormalities of which 17.5 was synaptic anomalies. They further indicated high frequency of mitotic chromosome abnormalities might be responsible for infertility in these patients.
The presence of abnormal human spermatozoa was observed by several workers. Presence of head-less human spermatozoa was noticed by Perotti and Gioria in 1981. Baccetti et al. (1984) and Baccetti et al. (1989) studied the morphogenesis of decapitated and decaudated spermatozoa present in the semen. They also observed 'Mimacroosme' sperm defect causing infertility in two brothers. In 1998 Chemes and others studied the ultra structure of the sperm flagella to associate with pathology and fertility prognosis. Chemes et al. (1999) reported the role of acephalic spermatozoa in the abnormal development of head–neck attachment causing impairment in the process of fertilization. Lilford et al. (1994) attempted to study whether oligoasthenoteratospermia has any familial component or not. However, they could not characterize the sperm abnormalities or explain the genetic mechanism of transmission.

Baccetti et al. (1997) correlated male sterility with sperm structure. Based on the submicroscopic study of sperm characteristics of infertile patients sperms could be classified into categories of apthologies, immaturity, necrosis, apoptosis and auto antibodies. Most of these are caused by infections, varicocele, hormonal alterations etc. The most common sperm defects are the following (1) Crater defect (2) Round headed defect (3)
Miniacrosome sperm defect also known as acrosomal hypoplasia (4) The stunted tails (5) Kartagener's syndrome (6) The detached tail (7) The 9+0 axoneme and (8) absence of axoneme.

Afzelius (1975) was the first to recognize relationship of Kartagener's syndrome with male infertility due to immotility of the spermatozoa. This immotility is due to defects in the dynein arms present in the sperm tail. Yokota et al. (1993) and Wolf et al. (1994) also established that the male patients were infertile because of the immotile sperms. Lilford et al. (1994) based on a case study has suggested a familial component for subfertility in men following the inheritance pattern of autosomal recessive gene. Rosa et al. (2001) indicated an association between translocation 3;22 in man leading to infertility and Nooman's syndrome.

The importance of sperm morphology in determining infertility was first proposed by MacLeod (1951) who compared the sperm morphology of both fertile and infertile men. In 1980 WHO published a manual for andrology laboratories for the correct assessment of man's fertility potential in which semen analysis was given due importance. Later in 1992 it was updated incorporating guidelines for sperm morphology evaluation for the diagnosis of human male infertility. In 1996, Eggert-Kruse proposed sperm morphology as a useful criterion in assessing male infertility. In 1996, Aziz et al.
suggested a sperm deformity index as a reliable prediction of outcome of oocyte fertilization. They also found sperm morphology more closely associated with fertilization rates than sperm count and motility of the sperms.

Hoodfar and Teebi (1996) made epidemiological studies of the consanguineous marriages in the Middle East and found that diseases associated with autosomal recessive disorders were more frequent among their children when compared with other population.

Sharon et al. (2001), while reviewing the semen quality and fertility observed a decrease in semen volume, percentage of normal sperms and sperm motility with increase in age. Ageing is not to be an important factor in affecting semen quality and semen volume. Schneider (1978) and Hamilton and Naftolin (1981) indicated that the decrease in the semen volume associated with increase in age could be caused by seminal vesicle insufficiency with increase in age because of the seminal fluid contributes most to the ejaculate volume. In addition changes in the prostate occurring with increase in age, smooth muscle atrophy, decrease in water content are other factors reducing semen volume. MacLeod (1964) suggested degenerative changes occurring in the germinal epithelium due to ageing may affect spermatogenesis and sperm morphology. Johnson (1986) suggested the narrowing and sclerosis
of tubular lumen might decrease the spermatogenic activity such as degeneration of germ cells and decrease in the number of functional Leydig cells. Martin et al. (1995) observed increased sperm aneuploidy with increase in age. A similar observation was also made by Modell and Kuliev (1990) where they noticed an increase in mutation rate in older people which resulted in foetal loss and genetic diseases of the offspring.

V. HORMONAL CAUSES AND ANDROGEN RESISTANCE

Genetic disorders affecting secretion and action of gonadotropins have also been reported to cause male infertility. Kallman et al. (1944) first reported a syndrome with arrested sexual development due to selective gonadotropin deficiency. Arbizu et al. (1983) observed that excessive expansion of the polyglutamine region leads to spinal and bulbar muscular atrophy associated with impaired development of the secondary sex characteristics, oligozoospermia, azoospermia, testicular atrophy and reduced fertility. Waldstreicher et al. (1996) noted significant diversity in the clinical presentation of which the most important was the complete absence of pubertal development, sexual infantilism and varying levels of hypospadius and undescended testis. Cassidy and Schwartz (1998) indicated Prader - willi syndrome as an example of hypothalamic disorder associated with symptoms such as obesity,
hypotonic musculature, mental retardation, hypogonadism, short hands and feet and micropenis. This disease was found to be caused due to disorder in the genomic imprinting due to a deletion of the proximal part of the paternally derived chromosome 15 q. Bhasin et al. (2000) suggested that infertility could also be caused by inactivating mutations of LH and FSH receptor genes whereby those individuals present hypogonadism and Leydig cell hypoplasia. Men with LH receptor mutation exhibited a variety of phenotypic abnormalities including feminization of external genitalia. Leydig cell hypoplasia caused primary hypogonadism and delayed sexual development. Hayrh et al. (2002) studied testicular histology of these patients and observed the absence of mature Leydig cell in the interstitium.

**INTRAUTERINE INSEMINATION**

Templeton et al. (1990) while studying the epidemiology of infertility in Aberdeen observed that involuntary subfertility is a common problem affecting about 15% of the couples. Although artificial insemination techniques of various forms have been practised for almost 200 years. Recently intrauterine insemination (IUI) alone, or in combination with controlled ovarian hyperstimulation (COH) have been gained wide acceptance for couples with unexplained or mild to moderate male factor infertility
These techniques have been found to increase the pregnancy rate of 10.5 - 17.9% per cycle. (Kaplan et al., 2000). Goverde et al. (2000) compared the pregnancy rates of IUI with COH and IVF alone and found that IUI should be considered the most cost effective treatment for unexplained male factor infertility. Philips et al. (2000) also observed that IUI is more attractive to both patients and clinicians because IUI is less invasive and requires less intensive monitoring, associated with lower risks of hyperstimulation and multiple pregnancy. In a randomized study made by Matorras et al. (2000) it has been observed that IUI with husband's spermatozoa, the cumulative pregnancy rate of >60% can be achieved by adopting initial protocol of three cycles of IUI prior to IVF. Cohlen et al. (1998) had also reported that IUI with COH significantly increased the probability of pregnancy. Dickey et al. (1999) suggested sperm quality assessment is necessary for successful intrauterine insemination. According to them the sperm concentration should be at least $5 \times 10^6$/ml containing at least $1 \times 10^6$ motile sperms for insemination. Miskryl and Michael (2002) observed a threshold of $2 \times 10^6$ sperms with 80% motility is sufficient for IUI. Cohlen et al. (2000) suggested that IUI is superior to timed intercourse (TI) in couples with male subfertility and unexplained infertility.
Although clomiphene citrate (CC) and or gonadotropins are generally used for COH in conjunction with IUI. Studies made by Cohlen et al. (1998) and Cohlen et al. (2000) observed an increase in probability of conception when gonadotropins were used for COH / IUI compared with the use of IUI only.

Studies made by Ragini et al. (1999) in 449 COH / IUI cycles with CC and gonadotropins indicated an increased cycle fecundity for double insemination performed 12 and 34 hours after HCG administration, as compared with 34 and 60th hours after HCG injection. Hendin et al. (2000) studied the effect of patient’s sperm characteristics in the live birth occurring after intra uterine insemination. Montanaro et al. (2001) studied the male and female factors in improving pregnancy rate by regression analysis studies. Van Waart et al. (2001) have also indicated the predictive value of sperm morphology in intra uterine insemination.