SECTION IV

DISCUSSION
Infertility is a common upcoming problem wherein approximately 8% of men of reproductive age seek medical attention for infertility problems. Of these, up to 10% are with reversible causes affecting their fertility potential; varicocele represents 35% of these cases (Esteves et al., 2011). As such, the male partner must be systematically evaluated in every investigation of an infertile couple (Esteves et al., 2011). Because 80% of couples are able to achieve pregnancy within the first year of attempting, a couple should only be diagnosed as infertile after one year of regular sexual activity without using a contraceptive method. Investigation is initiated earlier when risk factors are present, including advanced maternal (>35 years) or paternal age (>45 years), a history of urogenital surgery, cancer, cryptorchidism, varicocele, orchitis, use of gonadotoxins or genital infections, etc. (Esteves et al., 2011). The Andrologist is responsible for diagnosing, counseling and treating the underlying cause whenever possible. When there is no specific treatment he/she is still responsible for referring the patient to specialized assisted reproductive techniques (ART) center or, if the Andrologist is a member of an ART center’s multi-professional team, for extracting the male gamete from the testicle or epididymis (Esteves et al., 2011).

For healthy young couples, the probability of achieving pregnancy per reproductive cycle is approximately 20 to 25%. The cumulative probabilities of conception are 60% within the first 6 months, 84% within the first year and 92% within the second year of fertility-focused sexual activity (Kamel, 2010). Infertility is a common clinical problem affecting 13 to 15% of couples worldwide (WHO, 1984). The prevalence varies throughout different countries, being higher in the underdeveloped nations where limited resources for diagnosis and treatment exist.
In the United Kingdom, infertility is believed to affect one in six couples (Zargar et al., 1997). According to Kamel et al., (2010), it should be regarded as a public health problem, as it affects not only the health care system but also the social environment (Kamel, 2010).

In most of the studies, the research was concentrated either only on reproductive organs or on hormones in infertile males. **This is the first study that was conducted on anatomical, pathological and hormonal differences among fertile and infertile males using semen parameters as criteria and compared the fertility potential among different infertile subgroups.**

**Seminal manifestation**

In the present study we detected a decrease in semen volume among infertile subgroups evaluated. Indeed, published reports showed a decrease in semen volume with ageing (Ford et al., 2000; Kidd et al., 2001; Ng et al., 2004). In the studies where the analyses were adjusted for the period of abstinence there was a decrease in semen volume of 3–22% (Ford et al., 2000).

In our present study, sperm count was found to be significantly decreased in infertile males when compared with the controls and the negative correlation was also observed between age, BMI and total sperm count but not significant (**Table 4 and Table 6**). This finding reveals that our data accord with the previous studies on the effect of age and BMI on male fertility potential. Jensen et al., (2004) reported a higher prevalence of oligozoospermia in overweight and obese men compared with normal-weight men (24.4% vs. 21.7%). Kort et al., (2006) found that BMI correlated negatively with the total number of normal spermatozoa. Najafi et al., (2011, 2012) showed the similar result in Mysorepopulation. Central obesity in particular appears to be associated with a decrease in circulating androgen levels proportional to the degree
of obesity. Data on the effect of age factor on sperm count accords with the similar results obtained in previous studies (Eskenazi et al., 2006; Dunson et al., 2004). The main reason for non-significant values obtained for these factors in the present study could be due to a randomized sampling rather than a purposeful sampling.

In the present study sperm motility tended to decrease with age, indeed most studies have found a decrease in sperm motility with increasing age (Mladenovic et al., 1994; Auger et al., 1995; Hassan and Killick, 2003; Ng et al., 2004). Those studies that adjusted the results for the duration of abstinence reported statistically significant effects, such as negative linear relationships and decreases in motility of 0.17–0.6% for each year of age (Berling and Wolner-Hanssen, 1997; Kidd et al., 2001). Thus, the present study supports the conclusion based on the data from most others, that there is consistent evidence for a decrease in sperm motility with increasing age although this correlation is not significant.

**Sperm viability**

Present investigation showed that semen samples containing higher percentage of viable sperms were mostly with normal physical profile (Normozoospermia) whereas abnormal semen samples were with poor viable sperms. Thus, viability of sperm may be considered as an authentic and handy tool to assess male fertilizing potential specially when facility for other sophisticated techniques if not available.

Sperm morphology is a good indicator of the status of the germinal epithelium (Mladenovic et al., 1994; Bujan et al., 1996). Degenerative changes in the germinal epithelium may be due to ageing which may affect spermatogenesis and thus sperm morphology. The results of our study clearly demonstrate that there is a significant increase in the frequency of sperm morphological defects among infertile males when compared with the control group (Tables 8 and 9).
The biochemical constituents of seminal plasma were routinely studied are fructose and citric acid. Fructose, a readily glycolysable sugar, is produced in humans mainly by the seminal vesicle with a small contribution from the ampulla of the ductus deferens and is essential for spermatozoal metabolism and motility as an energy source (Schoenfeld et al., 1979). Absence of fructose indicates congenital absence of seminal vesicle mainly in case of azoospermia. In a patient with a low volume ejaculate, the absence of fructose indicates ejaculatory duct obstruction, seminal vesicle dysfunction or hypoplasia (Aumuller and Riva, 1992). In the present study fructose value and semen volume is normal for almost all infertile cases. This indicates neither of seminal vesicle agenesis in azoospermic cases nor ejaculatory duct obstruction in other infertile conditions.

**Age as a risk factor:**

Hassan and Killick (2003) stated that increased male age is associated with a significant decline in fertility (five times longer to paternity when aged> 45 years), which is independent of the woman’s age, coital frequency, and lifestyle effect, as well as the effect of other subfertility risk factors. In addition, paternity at older ages may have significant effects on the viability and genetic health of human pregnancies and offspring, primarily as a result of structural chromosomal aberrations in sperm. The evidence for sex chromosomal aneuploidy suggests that there may be about a doubling of the risk at the age of 50 years (Sloter et al., 2004).

Decreased fertility rates in aged males could be due to cellular, biochemical and molecular changes in spermatozoa that affect the fertilization by decreasing sperm motility and hampering the potential for undergoing the acrosome reaction and penetrating an oocyte. Robertson et al., (1982) have reported a gradual decline of male fertility associated with the age factor. Autopsies of men who died from accidental
causes showed narrowing and sclerosis of the testicular lumen, decreased in spermatogenic activity, increased degeneration of germ cells and decreased number and function of Leydig cells with increase age (Bishop, 1970; Johnson, 1986). Clinical studies suggest that age was associated with diminished semen volume, sperm motility and sperm normal morphology, but sperm concentration had minor affected by age (Schwatz et al., 1983; Kidd et al., 2001). Increasing paternal age was also found to be associated with delayed conception in fertile couples, especially after age of 25 years (Hull et al., 1996). In our study, the prevalence of azoospermia and oligospermia was higher in subjects between 41-50 years indicating that age can be a causative factor for such conditions that brings about diminished sperm count and this is in agreement with previous studies.

Effect of obesity as a lifestyle Factor:

Obesity is a major health issue and the relationship between obesity and male infertility has been described recently in many reports (Oliva et al., 2001; Magnusdottir et al., 2005; Nguyen et al., 2007; Mara et al., 2008). Also, men with high BMIs typically are found to have an abnormal semen analysis as well. Jensen et al. reported a higher prevalence of oligozoospermia in overweight and obese men compared with normal BMI (Jensen et al., 2004). However, they did not find any relationship between increasing male BMI and percentage of motile sperm. Kort et al., (2006) found that BMI correlated negatively with the total number of normal spermatozoa. They did not report on sperm count or morphology. In a recent study in India, the negative correlation was found between male BMI and sperm parameters like sperm count and motility (Najafi et al., 2011) and stated that obesity may lead to male infertility by increasing lipid peroxidation (Najafi et al., 2011).
In a trial to improve the semen quality it was reported that; reproductive hormone levels have been shown to normalize after weight loss (Norman et al., 2004; Koloszar et al., 2005). It remains, however, to be seen whether weight loss may also improve semen quality. Sallmen et al., (2006) stated that, hormone irregularities in men affect stimulation of the testicles that inhibit sperm production (Shome and Parlow, 1974) Several studies have reported reductions in testosterone with obesity (Jensen et al., 2004; Roudebush et al., 2005; Fejes et al., 2006). In massively obese individuals, reduced spermatogenesis associated with severe hypotestosteronemia may favor infertility (Ratcliffe et al., 1988; Sallmen et al., 2006). In another study, overweight and obese men had reduced sperm motility and increased sperm DNA fragmentation (Kort et al., 2006). Contrary to other recent studies, no increased risk was observed in the present study among obese men, could be due to the less sample size.

Many studies lacked information on frequency of sexual intercourse so obesity-related changes in sexual function could not be distinguished from obesity related effects on fertility (Sallmen et al., 2006), because obesity has been associated with both sexual and erectile dysfunction (Esposito and Giugliano, 2005). Therefore, reduced intercourse frequency could be a mediating factor by which obesity produces infertility. In this study we observed the relationship between frequency of intercourse and men’s BMI. But the association was negative thus; the mechanism that explains the BMI effect is likely to involve hormones rather than semen changes or sexual function. All previous studies mainly focused on the effect of obesity on male infertility but none of them assessed the incidence of obesity among infertile couples and as per our knowledge this study is the first in India which analyzed the prevalence of overweight and obesity in infertile couples.
Endocrine evaluation

Androgens play a crucial role in the development of the male reproductive organs, such as the testis, the epididymis, the vas deferens, the seminal vesicle, the prostate and the penis. The role of androgens is an important topic in the study of puberty, male fertility and male sexual function. The effects of androgen withdrawal have been well established through the experimental model of orchiectomy. A decrease in the weight of the epididymis has been commonly observed in animals that have had their testicles removed. In these cases, androgen replacement, even at supraphysiological levels, only partially restored the weight of the epididymis. The removal of the testicles causes the loss of androgens, but it is clear that this approach affected estrogen levels and other testicular factors that may affect the maintenance of epididymis (Robaire et al., 2006).

The formation and function of the epididymis is androgen-dependent. The principal androgen, testosterone is essential for the development of the internal sex organs and is derived from the Wolffian duct system, which consists of the epididymis, the vas deferens, and the seminal vesicle (Umar et al., 2003). Dihydrotestosterone (DHT), the 5α-reduced form of testosterone is involved in the development of the prostate and the external genitalia. Although testosterone is the predominantly active androgen during the first phase of the postnatal development of the epididymis, it is the effects of DHT that are important in the epididymal fluid of the mature epididymis. DHT can be produced locally in the epididymis by principal cells and is primarily found in the initial segment of the duct (Dacheux et al., 2005; França et al., 2005; Robaire & Henderson, 2006).

The actions of both testosterone and DHT are initiated through the intracellular receptor known as the androgen receptor (AR). DHT is the more potent androgen
among them. The AR is found in all male reproductive organs and can be stimulated by either testosterone or its more potent metabolite, DHT. The binding of either testosterone or DHT to the AR may regulate distinct androgenic effects in target tissues. Clinical syndromes, such as androgen insensitivity (AIS), illustrate the differential actions of testosterone and DHT (Umar et al., 2003). AR expression in the developing male genital tract occurs in a strict temporal pattern. It is first detected in the mesenchymal cells, then in the epithelial cells and then in both the epithelial and stromal compartments of the epididymis (Umar et al., 2003; O’Hara et al., 2011).

**Endocrine evaluation is suggested when the following scenarios are present:**

a) A sperm concentration of less than 10 million/mL  
b) Erectile dysfunction  
c) Hypospermia (volume 1 mL) or d) Signs and symptoms of endocrinopathies or hypogonadism. The minimal evaluation includes the assessment of serum FSH and testosterone levels, which reflect germ cell epithelium and Leydig cell status, respectively. If the testosterone level is low, a second collection is recommended along with free testosterone, LH and prolactin measurements. Isolated FSH elevation is usually indicative of severe germ cell epithelium damage.

Highly elevated FSH and LH levels, when associated with low-normal or below normal testosterone levels, suggest diffuse testicular failure and may have either a congenital (e.g., Klinefelter syndrome) or acquired cause. Concomitant low levels of FSH and LH may implicate hypogonadotropic hypogonadism. This condition may be congenital or secondary to a prolactin-producing pituitary tumor. Gonadotropin values within the normal range suggest an extraductal obstruction in azoospermic subjects. However, azoospermic patients with testicular failure and testis histology exhibiting sperm maturation arrest and 10% of those diagnosed with Sertoli-cell-only syndrome may present with non-elevated FSH levels. Serum estradiol levels should be
determined in patients presenting with gynecomastia. Infertile patients with a testosterone to estradiol ratio less than 10 can harbor significant but reversible seminal alterations (Raman and Schlegel, 2002). Vaucher et al., (2009) suggested that hyperestrogenism secondary to a higher conversion rate of testosterone into estradiol in Klinefelter syndrome (KS) patients inhibits testosterone production via a negative feedback pathway and may indicate the over expression of aromatase CYP19 in the testis. As such, there would be a scientific rationale for the use of aromatase inhibitors in KS patients (Raman and Schlegel, 2002). In azoospermic men with a normal ejaculate volume, FSH serum level greater than two times the upper limit of the normal range is reliably diagnostic of dysfunctional spermatogenesis (Technical Bulletin - American Society for Reproductive Medicine, 2008). Serum prolactin levels should be determined in infertile men with a complaint of concomitant sexual dysfunction or when there is clinical or laboratory evidence of pituitary disease; however, hyperprolactinemia is rarely a cause of infertility in healthy men (Sigman and Jarow, 1997). Although hormonal alterations may be present in approximately 10% of men who undergo assessment, clinically significant changes affect less than 3%.

In our study, decreased LH level was observed in 21 subjects of the infertile group and 6 subjects of the control group. Moreover, 43 infertile subjects and 11 subjects from control group expressed higher levels of LH values when compared with the normal ranges.

FSH levels was observed to be decreased in 19 infertile subjects and 3 control males while an increase of FSH were found in 56 infertile cases indicating more frequent germ cell epithelium damage than normal males.
In the present work we observed that the level of serum estradiol was found to be lower than normal values in 8 infertile subjects while 43 infertile subjects showed a significant increase in estradiol levels compared to the normal values that may indicate the higher conversion of testosterone to estradiol due to over expression of aromatase CYP19 in the testis.

With respect to the serum prolactin level, 4 infertile and 3 control males showed an increased levels of prolactin compared to the normal values. Higher number of infertile subjects (30 males) with decreased values for serum prolactin indicates more sexual dysfunction among infertile males.

In the present study, testosterone levels was found to be decreased in 61 cases of the infertile group and 10 cases showed an increase in testosterone level stating that most of the infertile cases show tendency towards decrease in testosterone level than increase. Among control group, 8 subjects showed a decreased value in testosterone levels and only 3 subjects showed increased testosterone level when compared with the normal range of the laboratory. All the data obtained in our study accord with the previous studies conducted for hormonal assessment of male infertility.

**Physical Examination**

Appropriate sexual development was assessed in physical examination. In the presence of diminished body hair distribution, gynecomastia or eunuchoid proportions, androgen deficiency was suspected. Genital examination in our study revealed the presence of a hypospadiac urethral meatus, pathologic curvature of the phallus or an active sexually transmitted disease. Normal adult testicles should have a length of 3.5-4.0 cm, breadth of 2.0-2.5cm and thickness of 2.5-3.0 cm, resulting in a volume of approximately 12-18cc. Testicular volume can be estimated using a pachymeter or an orchidometer. Testicles should present with a firm consistency. Approximately 85% of
the testicular parenchyma is involved in spermatogenesis, but there is no lower limit for testicular volume to exclude the presence of spermatozoa.

**Colour Doppler Ultrasound scanning and Trans Rectal Ultrasound Scanning (TRUS) of subjects for reproductive organs**

Physical deformities of the male reproductive tract are structural abnormalities that can damage or block the testes, epididymis, seminal ducts, or prostatic utricles and ultimately decrease fertility. These deformities differ in their pathological impact on male reproductive function; some render men totally sterile (such as bilateral absence of the vasa deferentia) while others produce only mild alterations in semen parameters (such as hydrocele). Other physical abnormalities, such as inguinal hernia, may not result in male infertility directly, but are commonly associated with other fertility-threatening conditions. Moreover, surgical repair of inguinal hernia can also result in male infertility.

**Colour Doppler scanning of the Scrotum Testicular scanning**

**Testes**

Assessment of testicular volume in relation to spermiogram in a sizable group of infertile men when compared to healthy fertile individuals once again confirms our insight into the changes of the testicular function in infertile males.

This study is, to our knowledge, the first to analyze in detail relationship between testicular volume, measured by ultrasonography, and spermiogram in large group of young infertile males. Testicular volume was significantly lower not only in infertile individuals but in the elderly compared with the young control group, due to aging process through which the spermatogenesis is compromised. This might reflect the existence of testicular pathology distinct from the normal aging, even though subjects with detectable causes of testicular failure were excluded. It is also possible
that these changes represent a range of age-related alterations in testicular function. In the present study, the most common age group affected was 25–35 years comprising around 70% of the cases similar to findings of Cardona et al., (2009) and 25% of the patients were below 25 years, whereas Cardona et al., (2009) found only 8% of the patients in this age group. This can be due to early age of marriage in India.

In the present study the ultrasonic testicular volume was positively correlated with sperm count, which is in accordance with previous studies on sperm quality and measurements of the testes (Takahara et al., 1987).

**Varicocele**

Varicocele is defined as abnormal dilatation and elongation of the internal spermatic veins and pampiniform plexus of the spermatic cord. Varicocele affects about 15% of the men in US population (Steeno et al., 1976). Despite the fact that most adult varicoceles (>80%) have no effect on male infertility (Green et al., 1984; Sylora and Pryor, 1994). Several studies suggest that a man with varicocele is at risk of subsequent loss of testicular function and fertility, regardless of normal semen analysis or documentation of previous fertility (Cozzolino and Lipshultz, 2001; Marmar, 2001). At the same time, varicocele is the most common correctable cause of male infertility, present in 40% of men with primary infertility and in up to 70% of men with secondary infertility (Kursh, 1987; Jarow, 2001). The WHO has reported that 1 in 4 men with abnormal semen parameters have a varicocele, compared with 1 in 10 men with normal semen parameters (WHO, 1992). Significant improvement in semen parameters after varicocele repair has been achieved in more than 50% of affected men (Dubin and Amelar, 1971).

Unilateral or bilateral clinical varicocele is associated with defective endocrine and exocrine testicular and epididymal functions, manifested by disordered semen
parameters include asthenozoospermia, teratozoospermia, oligozoospermia and azoospermia. Several studies have shown testicular endocrine abnormalities in infertile men with varicocele, marked by low serum inhibin B levels and low serum testosterone, although these endocrine changes have not been reproduced in others (Pirke et al., 1983; Younes, 2000; Mormandi et al., 2003; Goulis et al., 2011) Sperm dysfunction in patients with varicocele is characterized by elevated sperm DNA fragmentation index, a build-up of oxidative stress markers, inactive mitochondrial activity and abnormal acrosome reaction (Lacerda et al., 2011). Leydig cell dysfunction has been demonstrated in patients with varicocele, in correlation with a reduction in serum testosterone levels (although the levels remained within normal limits) (Hudson, 1996). Animal studies have demonstrated reduced intratesticular testosterone, despite normal serum testosterone level, which may jeopardize the functional and proliferate activity of androgen-dependent cells along the genital ducts, such as epididymal principle cells, seminal vesicle cells and prostate cells (Luo et al., 2011).

The pathophysiological effects of varicocele on testicular function are incompletely understood, although the rise in scrotal temperature attributed to poor venous return has been suggested to be an important mechanism. Adequate venous return is an important mechanism for testicular cooling, which is essential for the process of spermatogenesis (Goldstein and Eid, 1989). Testicular thermal injury occurs via alterations in RNA binding proteins and DNA within the sperm, leading to an increased rate of apoptosis (Fujisawa et al., 1989; Yin et al., 1997; Nishiyama et al., 1998). Experimental elevation of epididymal temperature enhances apoptosis and diminishes the storage capacity of this structure resulting in impaired spermiogenesis and changes in sperm count, motility and morphology (Bedford and Yanagimachi,
Oxidative stress has been suggested as another major mediator of varicocele-induced testicular injury. 80% of infertile men with varicocele and 77% of men with incidental varicocele have elevated seminal ROS concentrations (Sharma et al., 1999; Hendin et al., 1999). Excessive ROS generation associated with varicocele has been attributed to an increase in nitric oxide, superoxide anion and hydrogen peroxide production, released by inducible nitric oxide synthase and xanthine oxidase in the dilated spermatic veins, (Mitropoulos et al., 1996; Romeo et al., 2003), which could cause the high levels of sperm DNA damage commonly seen in patients with varicocele (Fujisawa et al., 1989; Yin et al., 1997; Nishiyama et al., 1998; Smith et al., 2006). Oxidative stress has also been linked to a decrease in the antioxidant defense system in seminal plasma observed in varicocele (Barbieri et al., 1999; Chen et al., 2001).

Some investigators suggest that varicocele causes increased hydrostatic pressure in the pampiniform plexus and venous stasis, which leads to testicular hypoperfusion and, consequently, testicular hypoxia and progressive atrophy (Benoff and Gilbert, 2001). Venous stasis also results in the insufficient removal or backflow of toxic substances from the kidney or adrenal glands. Testicular hypoperfusion and hypoxia can lead to release of vascular endothelial growth factor (VEGF) from Sertoli cells, Leydig cells, vascular endothelial cells and epididymal principal cells (Shiraishi and Naito, 2008), which can then inhibit spermatogonial proliferation and lead to increased vascular permeability, capillary angiogenesis and thickening of basement membrane and interstitial tissue, interfering with regulation of microcirculation (Korff and Augustin, 1999).

Larger varicoceles (grade II and III) are associated with a higher incidence of testicular growth arrest (Zenke and Turek, 2005) and higher levels of oxidative stress
markers (Mostafa et al., 2006). Nevertheless, no significant correlation has been demonstrated between varicocele grade and the severity of semen quality impairment (Diamond et al., 2007).

The impact of varicocele repair on male fertility has been assessed in many retrospective and prospective studies. A recent meta-analysis reported that varicocele repair—whether by microsurgical varicocele vein ligation, macroscopic open inguinal procedure, laparoscopic vein ligation or embolization of the varicocele veins—can significantly improve sperm count, sperm progressive motility and sperm ultrastructure (Baazeem et al., 2011). Moreover, varicocele repair can enhance sperm function through reduction in oxidative stress markers and DNA fragmentation index (Baazeem et al., 2011). Nevertheless, this meta-analysis failed to show significant improvement in spontaneous pregnancy rates after repair. Previous Cochrane meta-analyses have also failed to demonstrate improved paternity rates (Evers and Collins, 2001; Evers and Collins, 2007). Marmar et al., (2007) on the other hand, reported a significant improvement in pregnancy rate, which has been attributed to the inclusion of men with varicocele who were normospermic or had subclinical varicocele, a high patient dropout rate resulting in loss of paternity information, limited period of follow-up after repair, inclusion of prospective and observational studies in the same meta-analysis, and heterogeneity between studies. Future prospective studies are certainly required to critically assess the effect of varicocele repair on pregnancy rate, taking into account all these confounding factors.

Varicoceles are present in 15% of the normal male population and in approximately 40% of men presenting with infertility (Nagler, 1997). The preponderance of experimental data from clinical and animal models demonstrates a deleterious effect of varicoceles on spermatogenesis. Testicular temperature elevation
and venous reflux appear to play an important role in varicocele-induced testicular dysfunction, although the exact pathophysiology of varicocele induced damage is not yet completely understood. In our study, out of 274 infertile subjects, 8 (2.9%) of them were detected with right varicocele, 40 (14.6%) of them were found to be associated with left varicocele and 51 (18.6%) of them were detected with bile varicocele. In total 98 infertile subjects (36%) were diagnosed with different types of varicocele that accords with the previous studies.

**Hydrocele**

Hydrocele is an abnormal collection of fluid between the parietal and visceral layers of the tunica vaginalis. It is the most common cause of painless scrotal swelling (Rubenstein et al., 2004) with an incidence of 1–3% in full-term infants (Baskin and Kogan, 1999) and up to 30% in premature infants and those with delayed testicular descent. The incidence in adult males is approximately 1%, (Esposito et al., 2004; Al-Kandari et al., 2007; Lipshultz et al., 2007) although prevalence varies according to country. Hydroceles are bilateral in approximately 7–10% of affected men (Mihmanli et al., 2004). The imbalance between fluid production and absorption through tunical mesothelial cells is the underlying mechanism that is responsible for the formation of hydroceles. Hydroceles are classified as communicating or noncommunicating based on the patency of the processus vaginalis—a peritoneal pouch that invades and migrates with the gubernaculum to provide the potential space for the testis to descend into the scrotum (Heyns, 1987). The processus vaginalis normally closes after complete descent of the testis, within 18 months of birth. However, autopsy findings suggest that a patent processus vaginalis is present in 80–94% of infants and in 15–30% of adults (Skoog, 1997; Barthold and Kass, 2002). In the presence of a unilateral patent processus vaginalis, the incidence of a contralateral patent processus vaginalis
has been found to be 15–22% (Schneck and Bellinger, 2007). Hydrocele constitutes the third most common ultrasonographically-detected scrotal abnormality after varicocele and epididymal cyst (Pierik et al., 1999).

Communicating hydroceles occur when the processus vaginalis is persistently patent. They are commonly diagnosed in the pediatric age group and are frequently associated with indirect inguinal hernia when the patent processus vaginalis is wide. Diurnal variation in the size of hydrocele occurs owing to gravity-induced movement of the peritoneal fluid (Schneck and Bellinger, 2007). Although communicating hydroceles are less common in adults, they are sometimes observed in patients with a patent processus vaginalis accompanied by increased intra-abdominal fluid or pressure owing to shunts, peritoneal dialysis, or ascites (Barthold and Kass, 2002; Schneck and Bellinger, 2007). Adults with connective tissue disorders have a high risk of communicating hydrocele owing to attenuation of tissue support to the inguinal openings (Baskin and Kogan, 1999). Intrauterine exposure to polybrominated biphenyl, a brominated flame retardant and endocrine disruptor, is a risk factor for pediatric hydrocele (Small et al., 2009). Closure of the processus vaginalis results in a noncommunicating hydrocele. Depending on location, noncommunicating hydroceles are referred to as simple scrotal hydrocele (limited to the area surrounding the testis) or hydrocele of the cord (surrounding an isolated part of the spermatic cord). Noncommunicating hydroceles are more common in adults than children. Primary adult hydrocele is usually of idiopathic etiology, whereas secondary hydrocele can be caused by testicular torsion, tumor, infection, trauma or varicocelectomy (Kogan et al., 2002).

The impact of hydrocele on testicular geometry and size, spermatogenesis, scrotal temperature and testicular blood flow dynamics has been evaluated. Dandapat
et al., (1990) assessed the pressure effect of hydroceles in 120 men with unilateral idiopathic hydrocele, finding no pressure effect in 70% of men, testicular flattening in 22% of the cohort and pressure-induced testicular atrophy in 8% of patients. Turgut et al., (2006) noted time-related testicular size declines in patients with hydrocele and described a rounding rather than flattening effect of hydrocele on testicular shape (Turgut et al., 2006). By contrast, Mihmanli et al., (2004) found that testicular volume was larger in men with hydrocele and that the testis returned to normal size after hydrocele excision. They propose that this increase in size is due to hydrocele pressure-induced obstruction in the vessels of the testis, which creates stasis in the venous and lymphatic outflow resulting in testicular vascular edema (Mihmanli et al., 2004).

Some investigators have shown that hydrocele can affect spermatogenesis, which may be partially or totally absent (Dandapat et al., 1990; Mangoud et al., 1993). For example, Dandapat et al., (1990) reported normal spermatogenesis in 82% of the cohort, partial arrest of spermatogenesis in 10% and a total arrest in 8% (Dandapat, et al., 1990). The possible pathophysiologic mechanisms that underly impaired spermatogenesis include the pressure effect of the hydrocele on the testis, (Turgut et al., 2006) the reaction of testicular cells to the highly proteinaceous fluid, and raised intrascrotal temperature (Mihmanli et al., 2004).

The hydrostatic pressure of a hydrocele exceeds the pressure in blood vessels within the scrotum, which interferes with arterial blood flow and might have an ischemic effect on the testicle. Histopathologic testicular changes observed in patients with hydrocele include interstitial fibrosis, thickening of the basement membrane, and disorganization of spermatogenic cells (Bhatnagar et al., 1970; Singh et al., 1989; Dandapat et al., 1990; Mangoud et al., 1993). Testicular blood flow dynamics reveal an increase in the resistive index of the subcapsular arteries of the ipsilateral testis,
compared to those in the normal testis. Mihmanli et al., (2004) used color Doppler ultrasonography to assess blood flow before and after surgical excision of hydrocele, and found that a high-resistance flow in the intratesticular arteries before surgery was replaced by a low-resistance flow after hydrocele repair and elimination of the pressure. Nye et al., (1997) on the other hand, observed a lack of testicular diastolic flow ipsilateral to the hydrocele. Altered blood flow dynamics clearly indicate that hydrocele causes an ischemic insult to testicular tissue. Besides that, hydrocele repair may inadvertently injure the epididymis and vas deferens (Zahalsky et al., 2004).

In the present study, 68 infertile subjects (25%) were found with hydrocele out of 274 infertile subjects. Wherein 14 (5.1%) of them were detected with right hydrocele, 19 (6.9%) of them were found to be associated with left hydrocele and 35 (12.7%) of them were detected with bile varicocele. Certainly, controlled randomized trials are required to prove or disapprove such a relationship and to verify the usefulness of hydrocele repair for improving paternity rates in infertile men. In India and other tropical countries the incidence of hydrocele is much higher due to the high prevalence of filarial infections. In one review of 500 cases of hydrocele from India almost 43% were due to filarial infections (Kumar et al., 2006). Filarial infections are known to infect 120 million people worldwide and of these 25 million suffer from urinary and genital region infections. Hydrocele can also develop as a result of inflammation or injury within the scrotum. Inflammation may be the result of infection of the small coiled tube at the back of each testicle (epididymitis) or of the testicle (orchitis). The imbalance exist between fluid production and absorption through tunical mesothelial cells is responsible for the formation of hydroceles in few infertile patients in the present study. Apart from this Congenital hydrocele, scrotal injury and radiotherapy could be other causative factor in our study.
Epididymal deformities

Epididymal cysts are the most common epididymal mass, occurring in 20–40% of asymptomatic men (Leung et al., 1984). 75% of epididymal cysts are true cysts, meaning they are lined with epithelial cells and contain lymphatic fluid. The remaining are spermatoceles, commonly formed from obstruction of the efferent ductal system, which leads to cystic dilatation with fluid containing spermatozoa, lymphocytes, and cellular debris. True epididymal cysts can arise throughout the epididymis before and after puberty whereas spermatoceles almost always occur in the epididymal head of postpubertal men (Dogra et al., 2003). The two types are indistinguishable on ultrasonography, so the only means of differentiating epididymal cysts from spermatoceles is aspiration of the cystic fluid to assess for the presence of sperm (Munden and Trautwein, 2000).

The exact etiology of epididymal cysts is unknown; however, Wollin et al., (1987) have suggested they arise from vestigial remnants of the epididymis that no longer communicate with epididymal tubules. Cysts have been linked to diethylstilbestrol exposure, testicular dysgenesis syndrome and cryptorchidism. Because the epididymis is an androgen-dependent structure, it has been assumed that fetal exposure to diethylstilbestrol, dietary ingestion of phytosterogen and cannabis intake have a role in causing not only epididymal cyst but also other genital anomalies, such as hypospadias and undescended testicles (Paulozzi et al., 1999; Baskin et al., 2001). Others have hypothesized that vasal or epididymal obstruction leads to epididymal congestion, swelling and secondary cyst formation, (Jarvis and Dubbins, 1989) although direct measurement of hydrostatic pressure in the epididymis after vasectomy does not support this theory. Epididymal cysts can occur in association with genetic syndromes such as von Hippel–Lindau and cystic fibrosis (Leung et al., 1984).
1984). The etiology of spermatocele is also unknown, but is thought to be the result of a focal weakening of the external layer of an epididymal tubule, leading to formation of diverticula. The clinical significance of epididymal cysts and spermatoceles, as well as their association with male infertility has not yet been resolved. Spermatoceles have been described as ‘sperm retrieval reservoirs’ in men with obstructive azoospermia (Rados et al., 1996) but there have been no reports of a correlation between epididymal cysts and male infertility, even in those with bilateral epididymal cysts. Watchful waiting with regular follow-up has been suggested for both epididymal cyst and spermatocele, as long as they are small in size and produce no symptoms. Cyst excision and spermatocelectomy are recommended for abnormally large and painful lesions, although surgery is not without complications. Epididymal injury is a primary concern during excision surgery and has been diagnosed or suggested in 17–50% of patients who undergo spermatocelectomy (Chiari and Drujan, 1980; Zahalsky et al., 2004). Such injury can lead to epididymal obstruction (Chiari and Drujan, 1980). Additional postoperative complications are those typical of scrotal surgery, including hematoma, hydrocele, hematocoele, infection and testicular atrophy due to vascular injury. Kauffman et al., (2011) suggested the use of microscopic surgery to reduce the incidence of injury to the epididymis, especially during spermatocelectomy (Kauffman et al., 2011). Percutaneous aspiration and sclerotherapy have been attempted but are not advocated due to the risk of epididymal obstruction, chemical epididymitis and recurrence (Beiko and Morales 2001).

**In the present study**, infertile males were found with right epididymal cyst while 16 subjects were diagnosed with left cyst and 11 subjects with bile cyst. 11 infertile subjects showed an atrophy of left epididym that could be due to genetic factors or torsion, may be caused by obstruction of the tubes that carry sperm from the
testicles. The reason for these cysts development is unknown, but they usually develop as a result of sperm and/or other fluids accumulating at the head of the epididymis. An epididymal cyst is often preceded by either an injury to the groin area or infection called epididymitis.

**Vas deferens**

Congenital absence of the vas deferens (CAVD) is an uncommon entity with a reported prevalence range of 1%-2% in the male population (Durieu et al., 1997). Most of these cases are due to bilateral vas agenesis (1%-6%). Only 0.4% of male infertility cases have been attributed to CUAVD. The infertility in CUAVD patients is often due to obstruction of the contralateral vas deferens (Weiske et al., 2000). Renal agenesis is more commonly associated with unilateral vasal agenesis (73.7%) compared to the bilateral form (11.8%)(Weiske et al., 2000). CUAVD occurring with renal agenesis is due to an intrinsic Wolffian duct defect. Other renal anomalies associated with CUAVD are malrotation of the solitary kidney, multicystic kidney, ectopic kidney, and horseshoe kidney (Khan 2001). Anomalies of the seminal vesicles, ejaculatory ducts, cryptorchidism, and inguinal hernia have also been reported in association with CUAVD (Kolettis and Sandlow). It is commonly discovered either during an evaluation for infertility or during a vasectomy. Casals et al., (2000) showed that 38% of congenital unilateral absences of the vas deferens cases are associated with mutations in the CFTR gene. About 45% of these mutations were specific to congenital absence of the vas deferens (CAVD) and were not found in cystic fibrosis patients. In the present study out of 274 infertile cases only 3 cases were reported with congenital absence of vas deferens. Of these, all three of them are due to bilateral vas agenesis. Hence our data accords the previous work. CFTR gene mutational analysis was not done in the present study.
Prostate abnormalities

Widespread implementation of imaging techniques such as TRUS and endorectal MRI has increased the detection of cystic lesions of the prostate, which are thought to affect 0.5–7.9% of men (Hamper et al., 1990; Dik et al., 1996). Various methods of classifying prostatic cysts have been reported, such as whether they are congenital or acquired, or based on their position within the prostate (midline, paramedian or lateral). Most recently, Galosi et al., (2009) suggested a new model based upon anatomical site, embryological origin and pathological characteristics that classify cysts into six major types. There are two types of cyst (midline prostatic cysts and ejaculatory duct cysts) that can obstruct the ejaculatory ducts and lead to male infertility.

Midline prostatic cysts can be divided into three types: prostatic utricle cysts (previously called Müllerian duct cysts), cystic dilatation of the prostatic utricle and enlarged prostatic utricles. A prostatic utricle cyst results from failure of the Müllerian ducts to regress causing focal saccular dilatation (Mayersak et al., 1989) Located at the region of the verumontanum, these cysts may extend above the prostate or slightly lateral to the midline, and may grow into a large mass. Prostatic utricle cysts do not communicate with the urethra, therefore aspirations do not contain spermatozoa (Kato et al., 2002). This type of cyst affects 5% of men with obstructive azoospermia (Li et al., 2010). The condition is usually asymptomatic, but patients in the third or fourth decade of life (Nghiem et al., 1990) may develop irritative and obstructive urinary symptoms as well as hematuria, hematospermia, bloody urethral discharge, ejaculatory pain, urinary tract infection, epididymitis, infertility and constipation (Shabsigh et al., 1989). Cystic dilatation of the prostatic utricle (cystic utricle) arises due to obstruction of the junction between the utricle and the urethra (Kato et al., 2002; Kato
et al., 2005). Such cysts are therefore able to communicate with the posterior urethra (Nghiem et al., 1990). Typically, cystic utricles are smaller than prostatic utricle cysts, are strictly localized to the midline, and measure no more than 15 mm (along the longest axis). Both prostatic utricle cysts and cystic utricles can enlarge and compress both ejaculatory ducts resulting in altered semen parameters, and sometimes azoospermia. The third type of midline prostatic cyst is not technically a cyst but rather an enlarged or hypertrophied prostatic utricle that communicates freely with the prostatic urethra. Mainly detected in children and adolescents, enlarged prostatic utricles are frequently found in children with urogenital malformations, such as proximal hypospadias or virilization defects (Hinman, 1993). TRUS and cystourethrography usually reveal an enlarged prostatic utricle that is midline and posterior—the wide opening into the posterior urethra can be easily identified. This type of cyst does not typically obstruct the ejaculatory ducts (Mayersak, 1989).

Ejaculatory duct cysts originate from the Wolffian ducts and occupy a paramedian or median position in the prostatic gland above the level of the verumontanum (Galosi, et al., 2009). Such cysts can be congenital or acquired, with etiologies including partial distal obstruction caused by chronic infection, transurethral manipulation, tuberculosis or urethral foreign body (Ardill et al., 1990). Ejaculatory duct cysts can be unilateral or bilateral and are associated with obstructive azoospermia. When small, these cysts appear on TRUS as intraprostatic masses just lateral to the midline at the base and midline at the level of the verumontanum (Nghiem et al., 1990). When large, however, these lesions can mimic cystic utricles and prostatic utricle cysts. Clinical presentation depends on the size of the cyst; small cysts are usually asymptomatic while large ones can cause hematospermia, ejaculatory pain, azoospermia and male infertility (Littrup, et al., 1988; Nghiem et al., 1990).
In the present study, a considerable number of infertile subjects, 137 (50%), were found with a decreased values (< 12 cc) for prostate volume when compared to the normal ranges (12-20 cc) with different value of deviation from 0.2 cc to 8 cc. In control group also 14 subjects were diagnosed with prostatic hypoplasia with lower volume than normal ranges which needs further investigation to understand the mechanism leading to this condition. Although these control subjects have normal semen parameters, they were associated with some other clinical symptoms like hydrocele or testicular hypoplasia. As per our knowledge, this is the first report in south India revealing these conditions in infertile and fertile population. Causative agents include bacterial infections similar to those causing urinary tract infections, as well as *Neisseria gonorrhoeae*. A related complication of prostatic abscess is uncommon. Prostatic cysts usually result from an obstruction of prostatic ducts and fluid retention within the prostatic parenchyma. There are usually multiple cavitary areas within the gland which potentially connect with the urethra. Paraprostatic cysts are thought to originate from the blind-ended uterus masculinus, formed from the müllerian duct system. Microscopically, nodular prostatic hyperplasia consists of nodules of glands and intervening stroma. Most of the hyperplasia is contributed by glandular proliferation, but the stroma is also increased, and in rare cases it may predominate. The glands may be more variably sized with larger glands have more prominent papillary in folding. Nodular hyperplasia is not a precursor to carcinoma. (Homma et al., 1996). The mechanism for hyperplasia may be related to accumulation of dihydrotestosterone in the prostate, which then binds to nuclear hormone receptors which then trigger growth.
Seminal vesicle

The function of seminal vesicle is important for fertility. Estimation of fructose level is a simple method for the assessment of the seminal vesicular function. Measurement of seminal fructose has been used in almost all laboratories across the globe as a marker of the seminal vesicular function. The WHO includes the measurement of this sugar to assess the function of these glands (WHO, 2001). After ejaculation, fructose is consumed by the spermatozoa in a process named fructolysis. At higher sperm counts, the process will be stronger resulting in a low seminal fructose concentration. That is the reason that seminal fructose is higher in azoospermic and oligozoospermic than in normozoospermic or polyzoospermic men. This can be seen that the value of seminal fructose concentration is not appropriate as a marker of the secretory activity of the seminal vesicles, unless the influence of sperm count on the fructose concentration can be excluded. A lower level of corrected seminal fructose were observed in men with hypofunction of the seminal vesicles (Gonzales and Villena 1997) and either low serum testosterone levels or with an obstructive process at the seminal vesicles has been related to male infertility (Gonzales et al., 1988; WHO 2001). Subjects with hypofunction of the seminal vesicles have low sperm motility, which itself may cause infertility (Gonzales and Villena 1997). In the present study no significant difference exists between controls and infertile subject with reference to fructose level indicating seminal fructose is not involved in male infertility in the present study.

Ultrasonographic examinations are useful for the diagnosis of seminal vesicle dysfunction because it is one possible cause of sexual impairment. Schultheiss et al., (2008) showed that urogenital infections may affect sexual function by causing premature ejaculation and erectile dysfunction. However, there is no direct evidence
regarding the influence of seminal vesicle dysfunction on ejaculation and erection (Schultheiss et al., 2008). Nevertheless, some studies have indicated that prostate inflammation often involves both seminal vesicle (Vicari 1999; Vicari et al., 2006) and this could have multiple effects on sexual function.

In the present study, Ultrasonographic examination of seminal vesicle has revealed that the mean value of right seminal vesicle volume was 0.97±1.09cc in infertile group that was lower when compared with the control subjects (1.05±0.93) but the difference was not significant (p>0.05). Similarly, the left seminal vesicle was also found to be insignificantly higher in controls (1.05±0.95) than infertile group (0.95±1.12, p>0.05). The presence of cysts in the seminal vesicle is extremely rare, they must be considered in patients presenting with symptoms of chronic prostatitis, recurrent epididymitis and recurrent UTIs.

To our knowledge, this is the first study exploring the ultrasound characteristics of the seminal vesicle in infertile individuals in relation to control group. The lack of ultrasound data on seminal vesicle function in infertile subjects with control is of particular relevance given the increasing interest of the negative impact of seminal vesicle on sperm parameters and consequently on male reproductive functions.

Hence Ultrasonography (US) is a simple and noninvasive method of imaging wherein imaging of the upper urinary tract is extremely important in these patients.