

**An-Najah National University  
Faculty of Graduate Studies**

**Main Causes of Infertility among Men  
Treated at Razan Centers in West  
Bank: Retrospective study**

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## **Dedication**

*To the soul of my husband mother (Howriah)*

*To my beloved husband Aqel Salah for his encouragement, patience, and support during my study.*

*To My daughter Lara, and for both Meelad and Meela'a who were born during my study.*

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*Finally, but foremost, to my mother, father, sisters, and brothers.*

## الإقرار

أنا الموقعة أدناه, مقدمة الرسالة التي تحمل العنوان:

### **Main Causes of Infertility among Men Treated at Razan Centers in West Bank: Retrospective study**

### **الأسباب الرئيسية للعقم عند الرجال المعالجين في مراكز رزان للعقم في الضفة الغربية**

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### **Declaration**

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

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**List of Acronyms**

<b>Abbreviation</b>	<b>Explanation</b>
WHO	World Health Organization
LH	Luteinizing Hormone
FSH	Follicle-Stimulating Hormone
TDS	Testicular Dygenesis Syndrome
ASA	Anti Sperm Antibodies
MAGI	Male Accessory Gland Infection
BMI	Body Mass Index
IVF	In Vitro Fertilization

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**Abstract**

**Introduction:** Reproductive health in Palestine focused mainly on women health and ignoring the role of men, in spite of the important role that men are playing in reproduction and fertility which impact his family and environment

**Objective:** This study was carried out to investigate the main causes of male infertility in two infertility centers in West Bank.

**Methods:** A convenience sample of 627 medical records for Palestinian males diagnosed with infertility in Razan centers in Ramallah and Nablus governorates between 2007 and 2009 were retrospectively reviewed for the cause of their infertility.

**Results:** Male factor alone was accounted for 52% of infertility among couples, of these 522/627 (83.3%) had primary infertility and 105/627 (16.7%) had secondary infertility. The mean duration of infertility was  $5 \pm 3.99$  years and the mean age for male cases was  $33.5 \pm 7.24$  years. The most common causes among infertile men were, idiopathic infertility 237/627 (37.6%), varicocele 203/627 (32.4%), obstruction of the seminal tract 113/627 (18%), and hormonal problems 32/627 (5.1%). Least

common causes found were, medication 13/627 (2.1%), spinal cord injury 11/627 (1.8%), cryptorchidism 10/627 (1.6%), and testicular failure 8/627 (1.3%).

**Conclusion:** More than half of the infertile couples were from an idiopathic causes. Study results confirm that understanding about male reproductive function and the environmental factors that affect it is insufficient.

**Recommendation:** Further studies should be conducted to assess the environmental and lifestyle factors that contribute to idiopathic male infertility in West Bank.

**Keywords:** Male infertility; Primary infertility, Secondary infertility; Semen parameters; West Bank.

# **Chapter One**

# **Background**

## **Chapter One**

### **Background**

This chapter includes definition and types of male infertility; diagnosis of infertility in men; causes of male infertility; risk factors that are suspected to affect fertility in men; semen analysis values; study significance; study objectives; and finally the research questions.

#### **1.1 Definition and types of infertility**

Male infertility is a problem of the reproductive system, and the word infertility itself means no fertile, and that would be equivalent to sterility <sup>[1]</sup>, sterility means that a man is totally unable to have a child <sup>[2]</sup>. The World Health Organization (WHO) and the American Society for Reproduction Medicine Practice Committee defines infertility as no conception after at least 12 months of unprotected sexual intercourse <sup>[3,4]</sup>. Infertility can be permanent (irreversible) or subfertility which means the probability of spontaneous conception may be decreased <sup>[3]</sup>. All men who are sterile would be considered infertile, but not all men who are infertile are sterile, because an infertile man can father a child with medical help or with simple change in his life style <sup>[4]</sup>.

A man is responsible in about 20% of infertility among couples, and contribute to infertility with woman in another 30-40% <sup>[5]</sup>. Infertility can either be primary or secondary; primary male infertility is when the man has never impregnated a woman, while secondary male infertility is when a man has impregnated a woman irrespective of the outcome of the

pregnancy<sup>[3]</sup>. Men with secondary infertility, in general, have better chance of future fertility<sup>[3]</sup>.

Duration of infertility is defined as the number of months during which the couple has been having sexual intercourse without the use of any contraceptive method<sup>[3]</sup>. This indicator gives an important information about the couple's future fertility, if the duration of infertility of 3 years or less the couples have a better chance of future pregnancy, but if the duration has been longer, then there is a severe biological problem<sup>[3]</sup>. But in general couples tend to seek medical advice after a shorter duration of infertility.

## **1.2 Diagnosis of Infertility in Men**

The most important steps in diagnosis of infertile men are a careful history taking and a physical examination<sup>[6]</sup>. The past medical history of patients is very important because it contribute to the diagnosis in one-quarter of cases of infertility<sup>[3]</sup>. Specific childhood illnesses may result in problems in the reproductive system like failing of testes to descend that result in cryptorchidism, post pubertal mumps orchitis (mumps accompanied with swelling of one or both testis), time of puberty, surgical history, therapeutic medications, and systemic diseases<sup>[6]</sup>.

Physical examination is the second step in diagnosing abnormalities that causes infertility in men, measurement of height, weight, and blood pressure will give some information about systemic diseases<sup>[3]</sup>. Body hair distribution gives an indication of androgen production, breasts should be inspected to detect gynaecomastia (breast enlargement), examination

### **1.3.1 Sexual or ejaculatory dysfunction**

Difficulties with sexual intercourse or ejaculation are identified in about 2% of couples who have fertility problem <sup>[3]</sup>. Sexual dysfunction can be as a result of either inadequate erection or inadequate frequency of sexual intercourse, if the average frequency of vaginal intercourse is twice or less per month it is inadequate <sup>[3]</sup>.

Ejaculation to be considered adequate, it should occur intravaginally, ejaculatory disturbance may results from ejaculation that occurs outside the vagina, no ejaculation takes place, or from retrograde ejaculation <sup>[3]</sup>. Retrograde ejaculation is characterized by ejaculation into the bladder, because the bladder sphincter does not function properly <sup>[8]</sup>. Normally, the sphincter of the bladder contracts before ejaculation forcing the semen to exit via the urethra <sup>[8]</sup>. Retrograde ejaculation could be occurred as a result of congenital absence of the bladder neck, nerve damage, diabetes, surgical procedures, and spinal cord injury, the diagnosis mainly based on founding spermatozoa in post-coital urine <sup>[9]</sup>.

### **1.3.2 Immunological cause**

Sperm antibodies may be found in the semen of both fertile and infertile men <sup>[8]</sup>, but it is diagnosed as immunological cause of male infertility when 50% or more of motile spermatozoa are found to be coated with antibodies <sup>[3]</sup>. Sperm antibodies have been found in 3-7% of infertile men <sup>[8]</sup>, and these antibodies may impair sperm function and may cause

infertility in some men with impaired fertility like previous vasectomy, genital tract infection, and testicular injury or torsion <sup>[8]</sup>.

### **1.3.3 No demonstrable cause (Unexplained infertility)**

Unexplained infertility can describe 10 to 15% of infertile couples <sup>[10]</sup>. Male is diagnosed not having any demonstrable cause only if he has adequate sexual and ejaculatory function and the semen analysis is normal <sup>[3]</sup>. Normal semen parameters are of volume  $\geq 2$ cc, concentration  $\geq 20 \times 10^6$ /ml, morphology  $\geq 30\%$  normal, and motility  $\geq 50\%$  <sup>[3, 10]</sup>.

### **1.3.4 Isolated seminal plasma abnormalities**

If the patient has normal spermatozoa but has abnormalities in the physical, or biochemical, or bacteriological composition of the seminal plasma, or increased number of white blood cells in semen then the patient is diagnosed with isolated seminal plasma abnormalities <sup>[3]</sup>.

### **1.3.5 Iatrogenic causes**

When the abnormal spermatozoa are due to medical or surgical causes it called iatrogenic causes <sup>[3]</sup>. There are some drugs that interfere with fertility like Sulphasalazine and Nitrofurantoin both may cause impairment of sperm quality by direct toxicity, Colchicine and Niridazole can cause depression of fertility, Spironolactone may antagonize the action of androgen, Cimitidine may inhibit androgen effect <sup>[3]</sup>. Hormonal treatments with high doses of corticosteroids, androgens, antiandrogens, progestogens, estrogens, and anabolic steroids that are taken by athletes can

cause reduction in the gonadotropin secretion and lead to testicular atrophy<sup>[3]</sup>.

Cancer therapy for some diseases can have a deleterious effect on fertility especially irradiation in the genital region <sup>[3]</sup>, the degree of damage and suppression of spermatogenesis that occur as a result of treatment of malignancy depends on whether exposure occur before or after puberty, and the dosage and duration of exposure. If irradiation occurs during or after puberty the damage of germ cell is more severe <sup>[8]</sup>. Cytotoxic drugs such as cyclophosphamide that used for cancer chemotherapy, when used in high dose or in combination regimens can cause severe germ cell damage <sup>[8]</sup>. Other drugs can cause erectile potency or ejaculation dysfunction include some antihypertensives and tranquillizers <sup>[3,8]</sup>.

Short term use of cocaine is associated with increase in the sexual performance, but chronic use is related to impotence in men <sup>[11]</sup>. Marijuana also affects sexual function; chronic marijuana consumption can decrease sperm concentration <sup>[11]</sup>. In heroin addicts and methadone treated patients there are abnormalities in their semen analysis especially sperm motility and morphology <sup>[11]</sup>.

Several surgical procedures may influence the male fertility, testicular biopsy can result in a temporary suppression of spermatogenesis <sup>[3]</sup>, bladder neck incision; treatment of urethral valves; and prostatectomy can results in retrograde ejaculation <sup>[3]</sup>. Lumbar sympathectomy, hypospadias, epispadias, and vesicular exstrophy may cause ejaculatory

disturbances <sup>[3]</sup>. Hernia repair may cause damage to the vas deferens or leads to production of antisperm antibodies, and that may also occur after hydrocelectomy or any other genital or inguinal surgery like vasectomy <sup>[3]</sup>.

Many of systemic diseases can influence fertility in men, diabetes mellitus and neurological disease may cause erectile impotence and disorders of ejaculation <sup>[3]</sup>. Chronic respiratory tract disease is associated with disorders of the sperm flagellum, tuberculosis can impair sperm transportation by causing epididymitis and prostatitis <sup>[3]</sup>. Chronic liver and renal failure may result in infertility, hepatic cirrhosis can cause testicular damage and lead to testicular failure <sup>[8]</sup>. Also fever exceeding 38.5c may cause suppression of spermatogenesis for a period of up to six months <sup>[3]</sup>.

### **1.3.6 Congenital abnormalities**

Congenital abnormalities include a history of testicular maldescent, karyotype abnormalities, and azoospermia (sperm concentration is  $0 \times 10^6/\text{ml}$ ) due to congenital agenesis of the vasa deferentia <sup>[3]</sup>. Cryptorchidism (testicular maldescent) is the failing of the testis to descend normally from the abdomen in to the scrotum <sup>[8,12]</sup>. Correction of testicular maldescent can be done surgically after puberty in men up to 32 years of age; however men over the age of 32 are at greater risk of death from surgery than from testicular malignancy <sup>[3]</sup>.

Karyotype abnormalities like in Klinefelter's syndrome that characterized by the presence of one or a number of extra X chromosomes, and in Down syndrome that associated with moderate to severe reduction in

sperm production, also a number of rare complex genetic syndromes can affect fertility in men <sup>[8]</sup>. In case of Y-chromosome gene deletion, micro deletion are more prevalent in infertile individuals, and deletions can cause severe spermatogenic defects ranging from non obstructive azoospermia to oligozoospermia <sup>[13]</sup>.

X-genes also affect male infertility in X-linked genetic disorders like Kuhlman's syndrome.<sup>[12]</sup> Y-linked mutations can have adverse effects on spermatogenesis and normal sperm function, and it was found that men lacking expression of fertility genes of the Y chromosome are unable to make adequate function sperm <sup>[13]</sup>. The prevalence of these defects increases as the sperm count decreases <sup>[8]</sup>. Congenital defects of the vas deferens, seminal vesicles, and epididymis may obstruct sperm transport and these include congenital absence of the vas and seminal vesicles, which is most commonly due to cystic fibrosis <sup>[8]</sup>.

### **1.3.7 Acquired testicular damage**

Acquired testicular damage is recorded when the abnormal spermatozoa are caused by parotitis with orchitis <sup>[3]</sup>. Mumps occurring before puberty and mumps not accompanied by orchitis do not affect fertility <sup>[3]</sup>. The majority of men with previous bilateral mumps orchitis develop severe oligozoospermia or azoospermia, and therefore infertility that is irreversible <sup>[14]</sup>.

Testicular injury and testicular torsion can cause testicular damage<sup>[3]</sup>. Testicular trauma as a cause of infertility is rare, but severe injury

accompanied by tissue damage to the scrotum may cause disruption of the blood testis barrier and initiate antisperm antibody production <sup>[3]</sup>. Testicular torsion is also infrequent cause of infertility, and fertility problems that results from a testicular torsion may be prevented by early treatment <sup>[3]</sup>.

### **1.3.8 Varicocele**

Varicocele is a dilation of the testicular veins within pampiniform plexus of the spermatic cord that holds up a man's testicles <sup>[15,16]</sup>. Varicocele may cause infertility if it associated with abnormal semen analysis <sup>[3]</sup>, but the mechanism is unclear <sup>[16]</sup>. According to human report update (2001) varicocele is found in 15% of the general population including adolescents and adults <sup>[16]</sup>, but the prevalence of varicocele among men attending the infertility clinics range between 30 to 40% <sup>[17]</sup>. A study in 24 centers for the WHO found varicocele in 25.4% of men with abnormal semen compared with 11.7% of men with normal semen <sup>[18]</sup>. So, not all men who have varicocele are infertile, but varicocele is more prevalent in infertile men <sup>[15]</sup>. Varicocele occurs more frequently on the left side <sup>[16,17]</sup> in about 90% of cases <sup>[19,20]</sup>, and it is common in men with secondary infertility <sup>[18,21]</sup>.

The etiology of varicocele is multifactorial, the most common is the differences in the anatomy of the left and right spermatic vein, absence of valves in the spermatic vessels resulting in retrograde of the blood flow, and compression of the left renal vein causing a partial obstruction <sup>[15]</sup>. Treatment of varicocele can be done by either surgery or embolisation <sup>[21]</sup>.

In a review of literature in 2008 to evaluate the role of varicocele repair on male infertility it was found that varicocele repair is an effective treatment for selected patients and the most cost effective <sup>[22]</sup>. But in 2009 another review to the effectiveness of varicocele treatment on restoring fertility in men the authors found that there is no evidence that treatment of varicocele will improve fertility <sup>[23]</sup>.

### **1.3.9 Sexually transmitted diseases**

Sexually transmitted diseases and male accessory gland infection (MAGI) can impair male fertility by increasing the reactive oxygen species, or by causing inflammation lesions of the epididymis, or urthritis, or urethral strictures, or ejaculatory disturbance, or by stimulating anti sperm antibodies (ASA) <sup>[3]</sup>. It is hypothesized that infection with Chlamydia trachomatis, ureaplasma urealyticum, gram-negative bacilli, and mycobacterium tuberculosis results in accessory sex gland dysfunction and cause infertility <sup>[8]</sup>. Infertile men may have a high incidence of herpes simplex and human papilloma virus in their semen, the presence of human papilloma virus in their semen may have an affect on sperm motility <sup>[3]</sup>.

### **1.3.10 Endocrine causes**

The hypothalamus-pituitary endocrine system regulate the hormonal events that required to the normal testicular function. Hypothalamus stimulated the pituitary gonadotropins which are : Luteinizing Hormone (LH) stimulate the production of testosterone , and Follicle-Stimulating

Hormone (FSH) which stimulate the production of seminiferous fluid <sup>[8]</sup>. Normal levels of LH and FSH are necessary for maintenance of spermatogenesis, disorders of the pituitary or hypothalamus will cause inadequate gonadotropin stimulation of the testis and that will lead to problems with fertility <sup>[8]</sup>.

Disorders of sperm production may results from either diseases that affect the testis which called primary hypogonadism or from disorders of the pituitary or hypothalamus which called secondary hypogonadism <sup>[8]</sup>. In men with primary hypogonadism the gonadotropin levels are increased (hypergonadotropic hypogonadism), while in men with secondary hypogonadism gonadotropin levels are low or low to normal (hypogonadotropic hypogonadism) <sup>[8]</sup>. Measurement of FSH concentration is necessary to distinguish between hypergonadotropic and normo-or hypogonadotropic hypogonadism <sup>[8]</sup>.

Normal FSH concentration may indicate obstruction of sperm transport <sup>[3]</sup>. Elevated FSH concentration may suggest severe defects in spermatogenesis, but in men with reduced testicular volume and signs of hypoandrogenism with the presence of high FSH level may indicate primary testicular failure, but if FSH is not elevated in these men that may due to failure of the hypothalamo-pituitary function or to pituitary tumor <sup>[3]</sup>. Assessment of FSH level is not necessary in men with sperm concentration over 5 million per ml and normal testicular volume <sup>[3]</sup>.

Plasma testosterone level must be measured in men with signs of hypoandrogenism and in whom FSH is not elevated, and in men with sexual dysfunction <sup>[3]</sup>. Prolactin is measured in men with sexual dysfunction or in men with signs of hypoandrogenism, some medication are responsible about increased prolactin concentration <sup>[3]</sup>. Thyroid function must be assessed because hyperprolactinaemia may be associated with hypothyroidism <sup>[3]</sup>, thyroid hormone assessment should be performed in men with suspected thyroid dysfunction <sup>[3]</sup>.

### **1.3.11 Seminal abnormalities**

Idiopathic oligozoospermia is accepted if the sperm concentration is less than  $20 \times 10^6/\text{ml}$  but more than  $0 \times 10^6/\text{ml}$  and there is no other cause from the causes mentioned above <sup>[3]</sup>. Idiopathic asthenozoospermia in this case the sperm concentration is normal but there is a low proportion of spermatozoa with progressive motility and none of the other causes is applicable <sup>[3]</sup>. Idiopathic teratozoospermia requires normal sperm concentration and motility but low morphology, and also none of the other causes is applicable. Idiopathic cryptozoospermia is diagnosed if no spermatozoa are found in the fresh semen sample, but few are found after centrifugation<sup>[3]</sup>.

Obstructive azoospermia is diagnosed if the semen is azoospermia (no sperm are present in the semen) but the testicular biopsy reveals a full complement of spermatogenic in the seminiferous tubules <sup>[3]</sup>. While patient's with idiopathic azoospermia has low or normal testicular volume

and spermatozoa are absent in any of the seminiferous tubules, the patient's is diagnosed with idiopathic azoospermia when the azoospermia is of unknown origin <sup>[3]</sup>.

There is a strong evidence that most of the disorders of the male reproductive system such as testicular cancer; declining in semen quality; undescended testis; and hypospadias is of an antenatal origin as a results of disruption of embryonal programming and gonadal development during fetal life <sup>[24]</sup>. All these are symptoms of one underlying concept the Testicular Dygenesis Syndrome (TDS), TDS can also be caused by either genetic or environmental factors <sup>[24]</sup>.

#### 1.4 Semen analysis

Semen analysis is very important to all couples presented with infertility, the specimen is obtained after abstinence 2-3 days and it should be delivered to the laboratory within one hour of collection <sup>[20]</sup>. The normal semen analysis according to the WHO criteria are listed in Table 1.1 <sup>[3]</sup>.

**Table (1.1): The reference value of semen analysis**

Reference value	Value
Volume	$\geq 2.0$ ml
PH	$\geq 7.2$
Sperm concentration	$\geq 20$ million sperm/ml
Motility	50% or more motile, or 25% or more with progressive motility
White blood cells	$< 1 \times 10^6$ /ml
Morphology	$> 30\%$

It is not accurate to diagnose a male as infertile based solely on one semen analysis, because there is variability in sperm density from ejaculate to ejaculate. Thus, it is recommended that if an abnormality is found, analysis of semen should be repeated 2 to 3 times to determine the presence of male infertility <sup>[21]</sup>.

## **1.5 Risk factors of male infertility**

### **1.5.1 Age**

Age is an important risk factor for conception for both men and women. The peak rate of conception occurs at age 24 for both men and women and then after age 35 the rate begins to decline significantly <sup>[25]</sup>. Studies have shown that blood testosterone levels decline with age, and the risk of becoming infertile doubled in men who are over 35 years old compared with men who are under 25 years old, and five times longer to conceive at the age of 45 <sup>[26]</sup>. Production of testosterone hormone begins to decrease around the age of 40, sperm quality changes with aging, also there is a decrease in the semen volume, motility, and normal morphology <sup>[1]</sup>.

Studies showed that sperm concentration is stable, but the percentage of motility is the only parameter which decreases with age, and the fertilizing capacity does not seem to be decreased <sup>[27,28]</sup>. However another study found that not only motility decreased with age but also sperm concentration, with normal sperm morphology decrease after the age of 45 years <sup>[29]</sup>. In a study on a convenient sample of 55 healthy men ranging in age from 52 to 79 years old compared with a control group of men less than

52 years old found that older men had lower semen volume, with abnormal sperm morphology and reduce vitality <sup>[30]</sup>. Another large retrospective study from a representative European database provided evidence that paternal age is an important risk factor for infertility <sup>[31]</sup>. A study in Belgium by Mahmoud et al.<sup>[32]</sup> indicated that testicular volume of elderly males in their eighth decade was significantly less with 31% when compared with the young control group of 18 to 40 years old.

### **1.5.2 Obesity**

Several studies have shown that fertility decreased in overweight and obese women <sup>[33,34]</sup>. Similarly, obesity may play a role in men fertility. A study in US investigating farmers and their wives showed that 10 kg increase in the body weight may reduce fertility by nearly 10%, and the great effect for men with a body mass index (BMI) of more than 32 <sup>[35]</sup>. A significant reduction in the number of normal motile sperm has been observed among men with BMI over 25, it also found that men with excess fat in the thigh and suprapubic area have poor semen quality <sup>[36]</sup>. A Norwegian cohort study found that the risk of infertility is associated not only with high BMI but also with low BMI <sup>[37]</sup>.

### **1.5.3 Occupational exposure**

Among the factors thought to affect male infertility is the occupational exposure, it was found that there is no significant association between infertility and occupational exposure <sup>[38]</sup>. Another study conducted

in Lebanon had demonstrated that occupational exposure to harmful physical and chemical agents is associated with increase risk of male infertility <sup>[39]</sup>. Exposure to organic solvents at work associated with reduction in count of motile sperm <sup>[40]</sup>, a number of solvents that are used in industry may have an adverse effect on male reproductive function like carbon disulphide that had shown to affect semen quality but in low exposures had shown no effect <sup>[41]</sup>. Previous exposure to glycol ethers in work place associated with decrease in the semen quality <sup>[41,42]</sup>.

Furthermore, welding may reduce the quality and quantity of semen, likewise, occupations in which the workers exposed to heat they have reduced sperm count <sup>[42]</sup>. Also workers in agriculture or in a pesticide factory may experience a negative affect on reproduction <sup>[42]</sup>, Dibromochloropropane [DBCP] can cause testicular toxicity and reduce sperm production <sup>[42,43]</sup>. In men who exposed to Ethylene Di-Bromide [EDB] had decreased sperm count and increase number of abnormal sperm <sup>[42,43]</sup>, also insecticide have been found to have decreased sperm motility but there is no effect on fertility <sup>[42]</sup>. Dichloro-Diptenyl-Trichloro-ethane [DDT] is a type of pesticides can lead to decreased fertility and altered sperm counts <sup>[43]</sup>.

Industrial and construction workers presents with an increase infertility rates because of greater exposure to stress <sup>[43]</sup>, occupational stress was negatively correlated with the proportion of normal sperm <sup>[42]</sup>. Heavy metals like cadmium and lead reduce the quality of semen <sup>[43]</sup>, mercury can

concentrate in the testes beside other organs, mercury poisoning leads to infertility <sup>[43]</sup>. Furthermore, mercury and copper can interfere in spermatogenesis <sup>[43]</sup>.

#### **1.5.4 Exercise**

There are many health benefits of exercise, despite of that there are a conflict results about the effect of exercise on the male reproductive function. It was found that endurance training at highest level does not alter the male reproductive function <sup>[44]</sup>, and there is no significant effect in hormonal profile and sperm parameters except for sperm motility in the cyclist (riding a bicycle) it was observed lower sperm motility but that may attributed to physical factors <sup>[44]</sup>. The effect of vicious cycling was studied in another study and it was found that infertility was from the less common symptoms <sup>[45]</sup>. But recent study suggesting that long term strenuous exercise have a deleterious effect on semen parameters <sup>[46]</sup>, and also resistance exercise shows a significant decline in free and total testosterone<sup>[47]</sup>.

#### **1.5.5 Type of undertrousers and position**

Types of undertrousers affect the scrotal temperature, and semen quality. Wearing tight fitting undertrousers is associated with increased scrotal temperature (as opposed to wearing loose undertrousers or being naked). Note that left scrotal temperature is higher than right scrotal temperature <sup>[48,49]</sup>.

Also the position or activity has its impact on increasing the scrotal temperature, walking is associated with significantly lower scrotal temperature than sitting <sup>[48]</sup>, while driving for more than two hours continuously is associated with increasing the scrotal temperature <sup>[50]</sup>.

### **1.5.6 Drinking alcohol and caffeinated beverages**

Previous studies had found no association between alcohol consumption and male infertility <sup>[51,52]</sup>. Whereas another study found that alcohol consumption affected the reproductive system at all levels <sup>[53]</sup>. A recent study in Nigeria found a significant effect of alcohol consumption on infertility especially moderate to heavy alcohol intake <sup>[54]</sup>.

Drinking caffeinated beverages may interfere with fertility in men; a study showed that men who consume more than three cups of tea daily is associated with decreased fertility <sup>[52]</sup>. While another study found that there is no effect of caffeine on the semen quality and quantity <sup>[55]</sup>.

### **1.5.7 Smoking**

The effect of smoking on male infertility and semen quality has been investigated in many studies on fertile and infertile men, their results are conflicting: several studies showed that smoking had an adverse influence on the semen quality specially among heavy smokers <sup>[56-59]</sup>, a study in Singapore found that smoking increases the risk of infertility and there is no difference among the different smoking groups <sup>[60]</sup>.

On the other hand, a mini review of studies on the effect of smoking on semen parameters showed that smoking had limited effect on semen quality <sup>[61]</sup>, and another study found no significant effect of smoking cigarettes on semen quality <sup>[62]</sup>. Whereas, another study found that there is no association between male smoking and delayed conception <sup>[63]</sup>. A study was done on young men from five European countries concluded that maternal smoking may reduce semen quality and testis size while current smoking had no effect on semen quality <sup>[64]</sup>. So it is still not clear whether smoking or not affects semen quality and male infertility since human susceptibility may play an important role for this deference <sup>[8]</sup>.

#### **1.5.8 Laptop and cell phones**

Exposure for a long time on a laptop will increase the scrotal temperature and have a negative impact on sperm parameters <sup>[65]</sup>. Furthermore, using cell phones has been noted to have an adverse effect on male fertility due to decreased semen quality which paralleled of daily exposure to cell phones <sup>[66]</sup>. Another study found that use of cell phones decreased the actual percentage of the live sperm and this correlated with the duration of using these phones <sup>[67]</sup>.

#### **1.5.9 War and stress**

For the relation between the war and infertility; a study on the French veterans found that only 9% of the gulf veterans have fertility problems and it was not in a high frequency <sup>[68]</sup>, also in a review of literature on the reproductive health following the first gulf war it was

found that there is some evidence of risk associated with service in the gulf war <sup>[69]</sup>. However, when two studies were conducted in Lebanon it was found a strong relation between war and increased male infertility, that may due to exposure to toxins and stress <sup>[70,71]</sup>. Men under stress their semen parameters are significantly decreased <sup>[72,73]</sup>.

## **1.6 Study significance**

From the researcher visits to Razan Center which provides In Vitro Fertilization services (IVF), and talking to doctors responsible for treating patients with fertility problems. The researcher has come across the reality that there is a high number of infertility cases, especially those with male factors in recent years. So the researcher wants to conduct this study to assess the proportion of male factor alone among infertile couples and to investigate the causes of infertility among men that are diagnosed with infertility.

## **1.7 Study objectives**

### **1.7.1 Main objective**

The main objective of this study was to investigate the main causes of male infertility in West Bank between January 2007 and December 2009.

### **1.7.2 Specific objectives**

1. To assess the proportion of male factor alone among infertile couples.

2. To identify the main causes of male infertility among males seeking treatment at Razan centers (Nablus and Ramallah).
3. To assess primary and secondary male infertility from 2007 until 2009 and to compare it with demographic characteristics (age, marriage duration, infertility duration, occupation, and residency).
4. To identify the semen quality of cases in terms of the sperm concentration, total sperm output, sperm motility, sperm morphology, and semen volume.

### **1.8 Research questions**

1. What are the main causes of male infertility in West Bank
2. Is there a difference between the proportion of primary and secondary male infertility
3. Is there an association between type of infertility and demographic characteristics (age, marriage duration, infertility duration, occupation, and residency).
4. is there a difference between the infertile groups in term of; sperm concentration; total sperm output; and semen volume.

### **Summary**

Male infertility is the inability of a man to impregnate a woman after at least 12 months of unprotected sexual intercourse, and male infertility can be either primary or secondary.

WHO has proposed a guided classification for diagnosing causes of male infertility; there are many medical, iatrogenic, congenital, acquired, and idiopathic causes that can cause infertility in men. Semen analysis is crucial to recognize fertile and infertile men and at least two semen analysis is required to diagnose a man as infertile.

Certain environmental, occupational, and lifestyle factors was discussed that are suspected to interfere with fertility in men and normal spermatogenesis.

**Chapter Two**  
**Literature Review**

## Chapter Two

### Literature Review

This chapter presents international, regional, and national studies which investigate male infertility prevalence; causes; and semen parameters of the infertile men.

#### 2.1 Prevalence and causes of infertility

Infertility becomes a public health problem when its frequency exceeds 15% according to the WHO <sup>[74]</sup>. Globally, it is expected that around 50-80 million people (8-12 % of couples) experience some form of infertility in their lives <sup>[14]</sup>. There are large differences in prevalences of infertility among countries that might be due to differences in definitions and epidemiological designs <sup>[75]</sup>.

A survey in 1992 in the United States reported that 8.5% of married couples had infertility <sup>[76]</sup>, and this rate was similar to the rate among infertile couples in Northern Sweden (9%), of which 6% primary infertility and 3% secondary infertility <sup>[77]</sup>. While In Western Siberia it was much higher, 16.7% of couples were considered to be infertile <sup>[78]</sup>; 3.8% of all couples suffered from primary infertility and 12.9% had secondary infertility, and male infertility was 6.4% from the total prevalence. A population based study in United Kingdom found that the incidence of infertility among couples was 9% <sup>[79]</sup>

In Spain, 257 males were studied to the cause of their infertility, endocrine cause was found in 3.5% of cases, 30% were idiopathic, 17.9%

of cases had varicocele, 12.8% were associated to cryptorchidism, 8.9% to Klinefelter syndrome, and 6.6% were to exposure to toxic substances <sup>[80]</sup>. The aetiology of male infertility was studied in Kenya in 2005 on 43 men; 23% of the cases presented with signs of hypogonadism, 35% with signs of pain and swelling due to acute inflammation of the testes, 9% had prolactinaemia, 5% had signs gonadotropin, another 5% had varicocele, and 23% of cases had idiopathic infertility <sup>[81]</sup>. Similar study was conducted in Brazil on 822 men; 34.3% of the cases presented with varicocele, 31.6% idiopathic infertility, 10.3% seminal tract obstruction, 5.2% mumps, 4.5% pyospermia, 4.4% had systemic diseases, 4.1% testicular failure, 1.7% cryptorchidism, and 1.3% had ejaculatory dysfunction <sup>[82]</sup>.

In Northern Tanzania, 112 couples were evaluated for the causes of their infertility; 37.1% of them had primary infertility and 62.9% had secondary infertility, and male factor alone was found in 6.8% of cases <sup>[83]</sup>. In southeastern Nigeria also, 314 couples were evaluated for the causes of their infertility; of them 65% had primary infertility while 35% had secondary infertility and male factor alone was found in 42.4% of the cases <sup>[84]</sup>. A retrospective study in Northern Nigeria was conducted on 537 infertile men; primary male infertility was seen in 96% and secondary male infertility in 4%, about half (48.7%) of the cases had genitourinary tract infection. In addition azoospermia from testicular pathology was seen in 3.4% and obstruction to the vas or epididymis was seen in 14%, 45% had oligospermia resulting from testicular insufficiency while 11.4% had oligospermia due to seminal tract obstruction <sup>[85]</sup>.

The causes of infertility among 430 infertile couples were studied in Mongolia, about one quarter (25.6%) of the couples infertility was due to male factor and 18.8% of the couples infertility was diagnosed in both partners. The most common causes of male infertility were a history of sexual transmitted diseases (44.2%), previous testicular damage (33.5%), obstructive azoospermia (8.4%), MAGI (6.7%), and acquired testicular damage (5.4%)<sup>[86]</sup>. In China 7872 newly married couples were followed up to assess the prevalence of infertility among those couples, the prevalence of infertility was found to be 5.1% (after 24 months of unprotected sexual intercourse)<sup>[87]</sup>. A retrospective study was performed in Thailand between 1999-2004 on 172 infertile couples, revealed 61.8% of primary infertility and 35.6% of secondary infertility. The causes of infertility in this study were found in 55.6% in both partners, 19.4% in male partner and 17.5% in female partner, whereas 4.7% of couples had unexplained infertility<sup>[88]</sup>.

In Bangladesh two recent studies were conducted on infertile couples; the first study estimated the prevalence of infertility among couples which was 10%; of which 40% male, 50% female, and 10% involve both sexes<sup>[89]</sup>. The second study was conducted to find out the causes of couples infertility among them; primary infertility was present in 61.9% and secondary infertility in 38%, a positive male factor alone was found in 13% of couples and oligospermia was the most common cause of male infertility<sup>[90]</sup>. A study about primary infertility in Kashmir region in India on 250 couples found that primary infertility account for 15%, and male infertility alone was 22.4%<sup>[91]</sup>.

In Iran, three studies were conducted to determine the prevalence of infertility among couples; in 2004 in Tabriz city the prevalence of infertility was 3.3%; 2% as primary infertility and 1.2% as secondary infertility <sup>[92]</sup>. From 2004-2005 a study was conducted in all provinces of Iran to assess the prevalence of primary infertility, and it was found to be 3.4% <sup>[75]</sup>. In 2007 another study was conducted to explore the prevalence and the risk factors of infertility (after 24 months of unprotected sexual intercourse), the overall prevalence of infertility was 8% ; 4.6% as primary infertility and 3.4% as secondary infertility <sup>[93]</sup>.

In Turkey most studies focused on genetics and its relation to male infertility, a study was carried out on 208 patients who had either non obstructive azoospermia or severe oligozoospermia compared with 20 fertile men, the rate of genetic abnormalities among infertile men was 12.5% <sup>[94]</sup>. A survey in 2009 was conducted on 1935 males with severe male factor infertility to assess the genetic abnormalities among those men, the researcher found that the genetic abnormality rate increased with the severity of infertility <sup>[95]</sup>.

In Arab countries, a retrospective study in Saudi Arabia was performed on 230 testicular biopsies, 31.3% showed normal spermatogenesis, 39.1% of cases had germinal cell aplasia, 13% showed hypospermatogenesis, 10.9% showed maturation arrest, 5.2% tubular sclerosis, and only 0.5% had karyotypic abnormalities <sup>[96]</sup>. Sixty four infertile men were evaluated between the period of 2001-2005 in Kuwait; 38% of them were azoospermic while 62% were oligospermic, 50% of

oligospermic cases had varicocele, the most common cytopathology was sertoli cell-only-syndrome, and varicocele imbolization resulted in a significant rise in the sperm count in oligospermic patients <sup>[97]</sup>. Another study was held in Kuwait on the genetics of primary male infertility on 289 patients, the study showed that chromosomal anomalies and Y microdeletions were found in 10.4% of the infertile men in the study <sup>[98]</sup>.

A cross-sectional study in Qatar on married men revealed that there was a strong association between male infertility and diabetes mellitus, the prevalence of male infertility in men with type 2 diabetes mellitus was 35.1% <sup>[99]</sup>. Causes of infertility were studied for 250 couples in Iraq, 77.2% of whom had primary infertility and 22.8% had secondary infertility, male factor alone was found in 36.8% of the cases <sup>[100]</sup>. A study was carried out in a center for IVF in Yemen on 485 testicular biopsies, 33.8% of cases showed germ cell aplasia, 19.2% showed fibrosis, 20.4% had obstructive azoospermia, and normal spermatogenesis was found in 27.5% of cases <sup>[101]</sup>.

In a study to understand the medical causes of infertility among 710 Sudanese couples, primary infertility was 62.4% and secondary infertility was 37.6%; male factor alone was found in 36.2% of couples, female factor in 49.3%, 1.5% had a combination of male and female factor, and the cause was unexplained in 13% of couples <sup>[102]</sup>. In Cairo, 1488 infertile couples were followed up between the period of 1980-1989, primary infertility affected the majority of couples (70.7%) and secondary infertility affected about 29.3% of couples, 20.6% of couples had male factor alone and in

12.2% of couples both the man and his wife suffered of infertility <sup>[103]</sup>. Another study in Egypt found that there was a decrease in sperm quality and increase in ASA in patients with varicocele compared with men without varicocele <sup>[104]</sup>. Also a study in Syria was done to assess the association between ASA and unexplained infertility, found a strong association between ASA and unexplained infertility <sup>[105]</sup>.

Many studies were conducted in Jordan on reproductive health. One of these studies was about the prevalence of some abnormalities in male reproductive system, the study found that the prevalence of inguinal hernia and undescended testis were 3% and 0.5% respectively <sup>[106]</sup>. Another case control study compared men who were exposed to x-ray with another group that was not exposed, a significant association between exposure to radiation and male infertility was found <sup>[107]</sup>.

In Lebanon, five studies investigated male infertility, three of them about war and its effect on male infertility, the study found a strong relation between war and increased male infertility, this may be due to exposure to toxins and stress <sup>[70,71,108]</sup>. Another study about the occupational and environmental exposure to heavy metals as a risk factors for male infertility found that exposure to harmful physical and chemical agents is associated with increase risk of male infertility <sup>[39]</sup>. The last study regarded consanguinity and family clustering and its effect on male factor, this study demonstrated a significant association between consanguinity and family clustering of male infertility <sup>[109]</sup>.

A study in Israel investigated the prevalence of genital Chlamydia and mycoplasma infection in 135 infertile couples attending a male infertility clinic compared with 88 fertile couples, found that the prevalence of Chlamydia and mycoplasma was higher in infertile couples <sup>[110]</sup>. Two other studies dealt with risk factors of male infertility; the first being the effect of vicious cycling on urogenital disorders, and infertility was from the less common symptoms <sup>[45]</sup>. The other study investigated the association between male infertility and occupational psychological stress found that male infertility is associated with industry and construction jobs <sup>[111]</sup>. Many other studies that covered several topics about infertility in Israel including gene variation, in vitro fertilization, and assisted reproductive technology, from these; a study on genotyping of idiopathic oligospermic and azoospermic men, resulted in that Y chromosome microdeletion contributed to male infertility <sup>[112]</sup>.

In Palestine there are no studies available about the causes of male infertility or even for the prevalence of infertility in men or infertility in general at the national level. Whereas, there is only one study about time to pregnancy that was conducted in agricultural villages in Hebron on newly married couples, the researcher found that prolonged time to pregnancy associated with oldest age category for both genders <sup>[113]</sup>.

## **2.2 Semen parameters**

Recent studies about semen quality have provided conflicting evidence, some studies suggested that there is strong evidence that semen

quality is declined over the years. In Paris from 1973 through 1992 the seminal volume, the sperm concentration, and the percentages of motility and morphology of normal spermatozoa were measured in 1351 healthy fertile men, during that period there had been a decline in the concentration, motility, and morphology but there was no change in semen volume <sup>[114]</sup>. Another study on 577 men in Scotland provides that sperm concentration and motility decreased with age <sup>[115]</sup>. The same results were found in a study in India on 7770 subjects from the period between 1993 to 2005 provides that the sperm concentration, motility, and morphology were lower during 2004-2005 compared with 1993-1994 <sup>[116]</sup>. Also a study in Jerusalem conducted to investigate the changes in semen quality among men involved in infertile relationships between 1990 and 2000 found that sperm count and motility declined significantly among men treated by intrauterine insemination <sup>[117]</sup>.

While other studies have found no evidence of any changes, a retrospective review of semen analysis in USA in 1996 for 1283 men over 25 years, concluded that there was no decline in sperm concentration <sup>[118]</sup>. The same results found in an Indian study in 2003 that have analyzed semen analysis for the last eleven years <sup>[119]</sup>. In Israel, a retrospective study of semen parameters among healthy sperm donors in Jerusalem for over fifteen years found that there were no significant changes in semen concentration and motility, but there was an increase in the semen volume during the study period <sup>[120]</sup>.

Furthermore, seasonal variation affected the semen concentration. A study in Europe found that the highest sperm concentration observed during the winter season and the lowest counts observed at the summer season, while no seasonal variation was detected for sperm morphology <sup>[121]</sup>. Although another study showed that sperm concentration is highest in winter and lowest in fall, and greater percentage of sperm with normal morphology in winter also and the lowest in summer <sup>[122]</sup>.

Geographical regions can affect semen quality. A cross sectional study in four European countries (Denmark, France, Scotland, and Finland) found a significant differences in semen quality between the four European cities <sup>[121]</sup>. Another study was conducted in France to investigate if there is a difference in semen within state found that there is difference between the north and the south in the total number of sperm, the north had higher number of sperm compared the south <sup>[123]</sup>.

Evaluation for semen analysis in USA for male partners of women presenting for an infertility consultation, 52% of subjects had at least one sperm abnormality, of them 51% had abnormality in sperm motility, 18% in sperm concentration, 14% in sperm morphology, and 4% were azoospermic <sup>[124]</sup>. A retrospective study in Spain based on reviewing the seminogram forms from 571 clinical files for couples that seeked consultation for infertility from 1993 until 2001, of the 571 seminogram forms; 65% had alteration in the seminal parameters, 24% were azoospermic, 11.9% had asthenonecro-zoospermia, 11.6% had

hypospermia, asthenozoospermia in 8.9%, oligoastheno-zoospermia in 8.4%, hypoasthenozoospermia in 4.9%, cryptospermia in 2.8%, and hypooligoasthenoterato-zoospermia in 1.9% <sup>[125]</sup>.

In 1985 classification for semen, samples were done on 500 Nigerian male partners of infertile couples, of them 74.2% were normozoospermic while 16.2% were azoospermic, 5.6% were necrospermic, and 4.1% were asthenozoospermic. Moreover the degree of oligospermia was mild in 35.9%, severe in 23.2%, and very severe in 40.9% <sup>[126]</sup>. Another evaluation for semen parameters were done in Ibadan a region in Nigeria between 1990 and 1999 on 824 male partners of infertile couples, of which 27.3% of these subjects had abnormal semen analysis with; 27.8% had asthenozoospermia, 6.7% had azoospermia, 25.5% had oligoastheno-zoospermia, and 13.1% of the study subjects had oligoasthenoterato-zoospermia <sup>[127]</sup>. In 2006 another semen evaluation for 348 Nigerian men, of them 68% had semen abnormalities, 30% had single factor abnormalities while 38% had combined factor anomalies <sup>[128]</sup>.

## **Summary**

This chapter briefly presents the prevalence and causes of male infertility at the international and national level. Also studies about semen parameters was reviewed and provided conflicting results, some studies suggesting that semen quality is declined while others had found no evidence of any changes. The researcher's literature review showed no previous published studies in Palestine about infertility in men.

should be done to the penis, testes, epididymis, vasa defrentia, scrotum, varicocele, prostate gland and seminal vesicles <sup>[3]</sup>. Examination to the inguinal region should be done to examine scars that may indicate surgery or injury or infection <sup>[3]</sup>.

### 1.3 Causes of Male Infertility

WHO has proposed a guided classification for diagnosing causes of male infertility (figure 1.1) <sup>[3]</sup>. This diagnostic classification aims at therapeutic strategies rather than at academically detailed subclassification <sup>[3]</sup>. This scheme is of great importance as a basis for standardization, and for comparative multi-centre studies <sup>[7]</sup>.

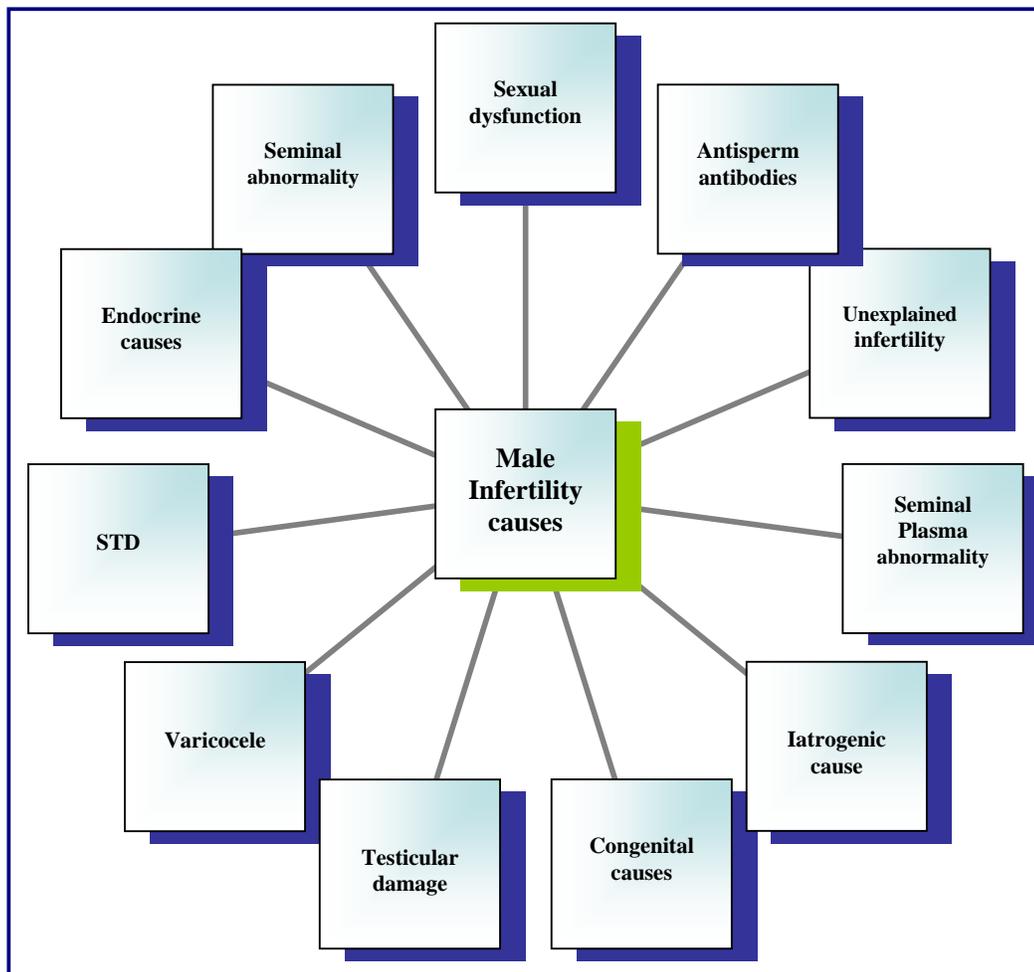


Figure (1.1): WHO diagnostic categories for male infertility causes

**Chapter Three**  
**Methodology**

## **Chapter Three**

### **Methodology**

This chapter specifies the steps used to carry out this study. In this chapter, the researcher presents the study design; study population and sampling; eligibility criteria; data collection; data analysis; and ethical consideration.

#### **3.1 Study design**

This is a retrospective cross-sectional study based on secondary data that was obtained from infertile men medical records from Razan centers in Nablus and Ramallah governorates that provide IVF services for cases from the different governorates of West Bank. Seven centers provide treatment for infertility in West Bank. These are; Razan, Al Hibah, and Al Amanah centers in Ramallah governorate; Alhanan, and Beit Ebrahim centers in Hebron governorate; Razan center in Nablus governorate; and Al Haia center in Bethlehem governorate.

Razan center was the first center in Palestine in the area of its specialization in terms of infertility treatment and in vitro fertilization that was established in 1995 in Nablus governorate. Another branch for Razan center was established in 2004 in Ramallah governorate. Razan center was chosen for this study because it is the first center in West Bank for infertility treatment, and had two centers one in Nablus governorate that covers the North of West Bank as there are no centers for infertility treatment in the North, and the second center in Ramallah governorate that

deals with cases from Middle and South West Bank. Also the center administrators had shown readiness to cooperate with this study.

### 3.2 Study population and sampling

The study targeted all married men who had problems with fertility and lived in West Bank, a convenience sample of available files of infertility cases who had been diagnosed between January 2007 until December 2009. A total of 1392 files were reviewed; 823 from Razan center in Ramallah governorate, and 569 files from Razan center in Nablus governorate, of these 723 files had male factor (Table 3.1).

**Table (3.1): Distribution of infertility cases by centers**

Centers	Male factor		Female factor		Unexplained		Combined male and female	
	N	%	N	%	N	%	N	%
<b>Razan center in Ramallah</b>	418	30%	177	12.7%	221	15.9%	7	0.5%
<b>Razan center in Nablus</b>	305	21.9%	92	6.6%	153	11%	19	1.4%
<b>Total</b>	723	51.9%	269	19.3%	374	26.9%	26	1.9%

From the 723 files of male factors, 96 files were excluded because these files include cases that were not residents in West Bank (24 files), or their duration of infertility less than one year (72 files). A total of 627 cases diagnosed with infertility male factor were covered by this study.

#### 3.2.1 Inclusion criteria

A case was included if he met the following criteria:

1. Married and resident in West Bank.

2. Had abnormal result of semen analysis, less than 20 million/ml according to the established WHO criteria <sup>[3]</sup>
3. Were trying to conceive for at least a year or more following an unprotected sexual intercourse.
4. His wife had no factors disrupt fertility.

### **3.2.2 Exclusion criteria**

A case was excluded if:

1. Wife had fertility problems.
2. Wife over 45 years-old of age, since older women experience decreased in their fecundability by more than 42% compared with young women <sup>[129]</sup>.
3. Cases with congenial abnormalities were excluded also because the center does not deal with these cases.

### **3.3 Data collection**

A compilation sheet (Annex A) was developed for this study after taking an oral permission from the general director of Razan center to inspect the information existing in the cases medical records. The compilation sheet contained three parts; the first part contained demographic characteristics regarding age for husband that ranges from 20-77 years old, age for wife that ranges from 17 to 45, residence (urban, rural,

refugee camp), and occupation for man. The second part contained data about marriage duration, infertility duration, type of infertility, number of children and abortion, past medical history, and cause of infertility. The last part contained the results of semen analysis, and the subject was classified as infertile based on semen count less than 20 m/ml on at least two tests. All semen analysis tests were conducted in Razan laboratories and data about semen parameters were gathered for total sperm count, semen volume, motility, and morphology. Analysis was performed by specialized trained laboratory workers according to the WHO laboratory manuals.

Cases were classified according to the interpretation of WHO to the results of semen analysis into the following categories <sup>[3]</sup>:

- Cryptospermia: if there is no sperm detected during routine semen analysis and few are detected after centrifugation.
- Necrospermia: if the sperm are dead.
- Azoospermia: if the concentration is  $0 \times 10^6/\text{ml}$ , and no sperm are detected after centrifugation.
- Aspermia: semen volume is 0 ml.
- Oligoasthenoterato-zoospermia: disturbance of all three variables (concentration, motility, and morphology).
- Oligozoospermia: divided into four categories:
  1. Mild oligozoospermia: ( $10 < 20 \times 10^6/\text{ml}$ )

2. Moderate oligozoospermia: ( $5 < 10 \times 10^6/\text{ml}$ ).
3. Severe oligozoospermia: ( $1 < 5 \times 10^6/\text{ml}$ ).
4. Extreme oligozoospermia: ( $< 1 \times 10^6/\text{ml}$ ).

The researcher herself collected the information from the cases medical records between May to July 2010.

### **3.4 Data analysis**

Following data collection, data were analyzed using Statistical Package for Social Sciences (SPSS) version 17. Comparisons between types of infertility and other categorical variables were made using Chi-Square test but when the table contains cells with expected counts less than 5 Fisher's exact test becomes more appropriate. The Kolmogorov-Smirnov test of normality was done to infertility duration, marriage duration, sperm concentration, sperm output, and to semen volume, in order to test if these continuous variables are normally distributed or not. The Kolmogorov-Smirnov test showed that all the five variables deviated from normality ( $p < 0.05$ ) so Mann-Whitney U test was used if the variable had two groups and when the variable had more than two groups Kruskal-Wallis test was used. Means, frequencies, and ranges were computed for continuous variables. All P-values were two-sided and considered to be significant if  $p < 0.05$ .

### **3.5 Ethical consideration**

The study has been approved by the Institutional Review Board (IRB) of An Najah National University. Confidentiality was taken into consideration regarding data obtained from cases medical records. As all cases were kept anonymous without names and just given codes for data analysis purpose.

### **Summary**

This retrospective cross-sectional study was conducted at Razan centers in Nablus and Ramallah governorates, and based mainly on secondary data obtained from cases medical records. A convenience sample of 627 records for cases diagnosed with infertility have covered this study. A compilation sheet was developed by the researcher after inspecting the information existing in the cases medical records which contain information with regards to; demographic characteristics, marriage and conception, and results of semen analysis. Data were analyzed using SPSS version 17.

## **Chapter Four**

# **Results**

## Chapter Four

### Results

This chapter presents the study results in accordance to the study objectives. It includes the demographic characteristics for the infertile groups; causes of male infertility; and seminal characteristics for infertile cases.

#### 4.1 Demographic characteristics of the infertile groups

This study found that the total number of infertile men during the study period (January 2007 to December 2009) was 627. There were 83.3% with primary infertility (a man had never impregnated any woman), and 16.7% of cases with secondary infertility (a man had in the past impregnated at least one woman irrespective of the pregnancy outcome). Table 4.1 shows some of the demographic characteristics for primary and secondary infertility groups.

**Table (4.1): Demographic characteristics of the infertile groups**

Variable	Primary infertility 522 (83.3%)	Secondary infertility 105 (16.7%)	P-value	Total 627 (100%)
	Mean $\pm$ SD	Mean $\pm$ SD		Mean $\pm$ SD
Men age	32.7 $\pm$ 6.76	37.3 $\pm$ 8.32	*0.000	33.5 $\pm$ 7.24
Wives age	26.6 $\pm$ 5.13	31.0 $\pm$ 5.38	*0.000	27.3 $\pm$ 5.43
Marriage duration	4.72 $\pm$ 3.95	8.74 $\pm$ 5.18	*0.000	5.39 $\pm$ 4.44
Infertility duration	4.72 $\pm$ 3.95	6.27 $\pm$ 3.95	*0.000	4.98 $\pm$ 3.99

Note: Mann-Whitney U test was used for all variables.

\*statistically significant at  $p < 0.05$

The mean age of all infertile men was 33.5 years old. ranged between 20-77 years. Men in the primary infertile group were significantly younger than men in secondary infertile group (33 versus 37 years;  $p < 0.001$ ). The mean age for wives was 27 years old, and wives of cases in primary group was significantly younger than wives of cases in secondary group. Marriage mean duration for primary and secondary infertile groups were 5 and 9 years respectively, the difference was statistically significant ( $p < 0.001$ ). The mean infertility duration was also significantly different between the primary (4.7 years) and secondary (6 years) groups ( $p < 0.001$ ).

Table 4.2 showed the rest of the demographic characteristics between infertile groups. The cases were from two infertility centers; 38.3% were from Razan center in Nablus district and 61.7% were from Razan center in Ramallah district. The proportion of primary infertile group treated in Ramallah center was 50.1% of all cases during the study period, also the percentage of secondary infertile group in the same center was twice (11.6%) than those in Nablus center (5.1%). Although the cases in Ramallah center are much more than the cases in Nablus center, there is no significant difference between centers and infertile groups ( $p = 0.071$ ).

In 2008 there was an increase in the infertile cases compared with 2007, while in 2009 the number of cases returned to decrease. Primary male infertility decreased in 2008 compared with the previous year and returned to increase in 2009. While secondary male infertility increased in 2008 and returned to decrease in 2009. The results of Chi-square test showed no significant difference between infertile groups and years of study ( $P = 0.113$ ) (table 4.2).

**Table (4.2): Relationship between infertile groups and study demographic characteristics**

Demographic characteristics	Primary infertility		Secondary infertility		P-value	Total	
	N	%	N	%		N	%
<b>Center</b>	522	83.3%	105	16.7%	0.071	627	100%
Nablus center	208	33.2%	32	5.1%		240	38.3%
Ramallah center	314	50.1%	73	11.6%		387	61.7%
<b>Year</b>	522	83.3%	105	16.7%	0.113	627	100%
2007	151	82.1%	33	17.9%		184	29.3%
2008	183	80.3%	45	19.7%		228	36.4%
2009	188	87.4%	27	12.6%		215	34.3%
<b>Age group</b>	522	83.3%	105	16.7%	*0.000	627	100%
<30	220	35.1%	26	4.1%		246	39.3%
30-34	135	21.5%	13	2.1%		148	23.6%
35-40	112	17.9%	35	5.6%		147	23.4%
>40	55	8.8%	31	4.9%		86	13.7%
<b>Governorate</b>	522	83.3%	105	16.7%	0.509	627	100%
Nablus	78	12.4%	11	1.8%		89	14.2%
Jenin	59	9.4%	9	1.4%		68	10.8%
Tubas	12	1.9%	3	0.5%		15	2.4%
Salfit	18	2.9%	3	0.5%		21	3.3%
Qalqilya	18	2.9%	3	0.5%		21	3.3%
Tulkarm	33	5.3%	2	0.3%		35	5.6%
Ramallah	100	15.9%	22	3.5%		122	19.5%
Bethlehem	36	5.7%	7	1.1%		43	6.9%
Hebron	107	17.1%	27	4.3%		134	21.4%
Jerusalem	50	8.0%	14	2.2%		64	10.2%
Jericho	11	1.8%	4	0.6%	15	2.4%	
<b>Locality</b>	522	83.3%	105	16.7%	0.949	627	100%
Urban	213	34%	44	7.0%		257	41%
Rural	272	43.4%	53	8.5%		325	51.8%
Camp	37	5.9%	8	1.3%		45	7.2%
<b>Occupation</b>	522	83.3%	105	16.7%	*0.000	627	100%
<sup>a</sup> Employees	111	17.7%	28	4.5%		139	22.2%
<sup>b</sup> Workers	180	28.7%	19	3.0%		199	31.7%
Teachers	14	2.2%	6	1.0%		20	3.2%
Health professionals	11	1.8%	3	0.5%		14	2.2%
<sup>c</sup> Artisans	41	6.5%	8	1.3%		49	7.8%
Drivers	32	5.1%	4	0.6%		36	5.7%
Unemployed	44	7.0%	15	2.4%		59	9.4%
<sup>d</sup> Business owner	51	8.1%	17	2.7%		68	10.8%
Military employees	30	4.8%	3	0.5%		33	5.3%
Farmers	8	1.3%	2	0.3%		10	1.6%

**Note:** Analysis was conducted using the Chi-squared test for all variables

\*statistically significant at  $p < 0.05$

<sup>a</sup>Employees: office employees

<sup>b</sup>Workers: group of men who do not have a craft and work in any job available to them.

<sup>c</sup>Artisans: painter, blacksmith, sewer, barber, bricklayer, ironer, electrician, carpenter, chef, butcher, confectioner, grease-monkey, contractor, and radio technician.

<sup>d</sup>Business owner: owners of a factory, restaurant, shopkeeper, office, or a trader.

The highest percentage of infertility (39.2%) was found among men who are less than thirty years old, followed by men aged from 30 to 40 (23.6%), while the lowest percentage (13.7%) was found among men who are over 40 years old. According to data presented in table 4.2, the percentages of infertility cases in general decreased with age, Chi-square test showed a significant difference between primary and secondary male infertility and age groups ( $p < 0.001$ ). Primary infertility is higher in men less than 30 years followed by men who were between 30 to 35 years. While according to secondary infertility we noticed that the age group from 35 to 40 years was the highest age group followed by men aged over 40 years old.

Cases of infertility were from the different governorates of West Bank. According to data presented in table 4.2, Hebron had the largest percentages of infertility cases in both types of male infertility (17.1%, 4.3%) respectively, followed by Ramallah (15.9%, 3.5%), Nablus (12.4%, 1.8%), Jenin (9.4%, 1.4%), Jerusalem (8%, 2.2%), Bethlehem (5.7%, 1.1%), and Tulkarm (5.3%, 0.3%). The rest of the governorates had almost the same proportions. Fisher's Exact test showed no significant relation between infertility groups and governorates ( $P = 0.509$ ).

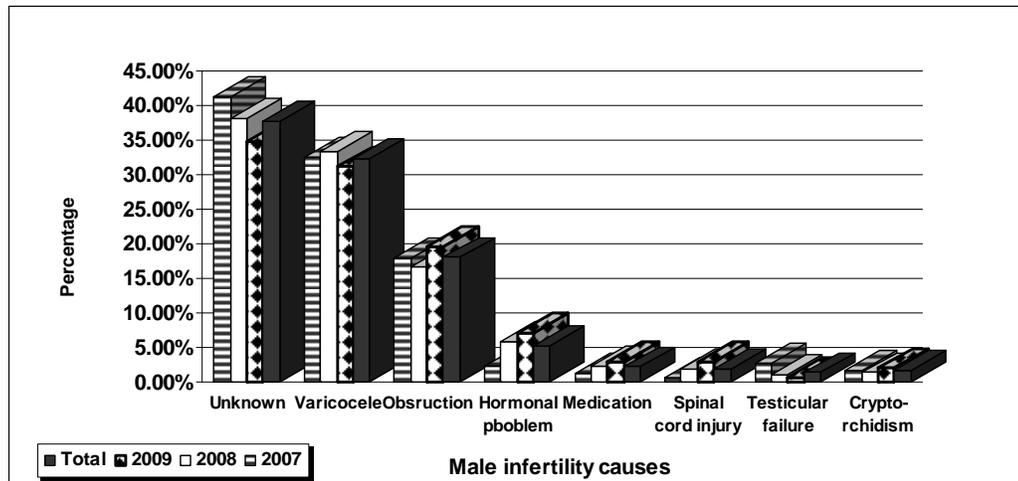
Half of cases (51.8% ) were residents primarily in rural areas, 41% in urban areas, and only 7.2% in refugee camps (table 4.2). The percentages of primary and secondary infertility were highest in rural areas, otherwise the percentages of secondary infertility in rural areas were comparable to

that in urban areas. But statistical percentages were not significantly different ( $p=0.949$ ).

According to occupation, workers made up the largest group (31.7%), followed by office employees (22.2%), business owners (10.8%), unemployed (9.4%), artisans (7.8%), and drivers (5.7%). Workers and office employees were most frequent among men with primary infertility. Employees, workers, and business owners were the most frequent among men with secondary infertility. Fisher's exact test showed a significant relation ( $p<0.001$ ) between infertility types and male occupations.

#### **4.2 Causes of male infertility**

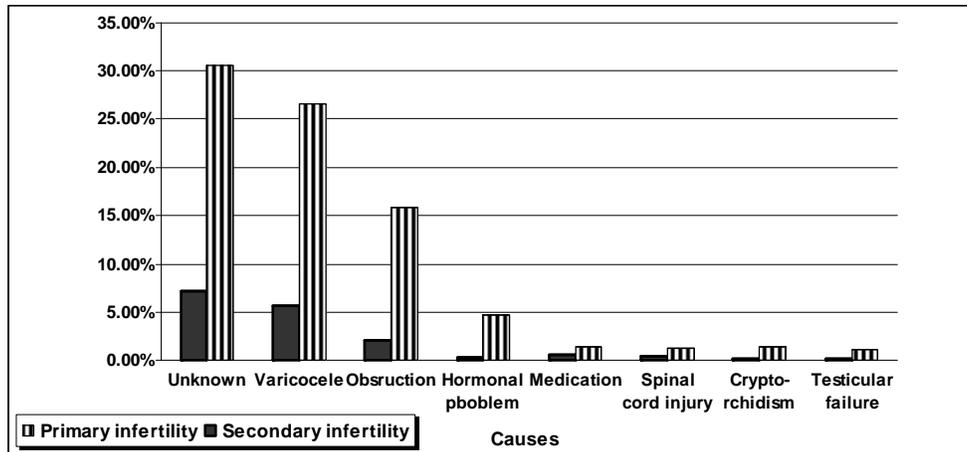
In this study there were eight main causes for infertility in men, figure 4.2 presents the distribution of male infertility causes according to year. The largest single cause during the study period was seminal abnormalities of unknown cause (37.8%). Beyond this, varicocele was the second largest cause and accounted for 32.4% from all causes. Of this ratio left varicocele was 70%, bilateral varicocele was 28.5%, and right varicocele was 1.5%. Seminal tract obstruction (obstructive azoospermia) and hormonal problems were relatively common 18%, 5.1% respectively. However, medication (2.1%), spinal cord injury (1.8%), cryptorchidism (1.6%), and testicular failure (1.3%) were very infrequent.



**Figure (4.1): Causes of male infertility according to year**

We also note that more than half of male infertility cases (58.4%) had a medical cause [varicocele, hormonal problems, cryptorchidism, obstruction, and testicular failure] for their infertility, while 37.8% had unknown cause, 1.8% of cases had exposed to accidents, and 2.1% of cases taking medication that affects their fertility. The vast majority of male infertility cases had one cause for infertility, while only 5.4% had two or more than two causes.

Primary infertility accounted for approximately 83.3% from all male infertility cases. So we noticed from figure 4.3 that primary infertility was higher in all causes, without exception, compared with secondary infertility. The results of Fishers exact test showed no significant differences between causes according to infertility groups ( $p=0.122$ ).



**Figure (4.2): Distribution of male infertility causes according to infertile groups**

Causes of male infertility varies quite markedly across the governorates. As shown in table 4.3 in Northern governorates we noticed that cases with medical causes accounted for nearly 28%, and this percentages was comparable to the southern governorates, while according to unknown causes southern governorates were much higher than the north by four folds. Hebron and Ramallah had the higher percentages in unknown and medical causes, Fisher exact test showed a significant relation between the causes of male infertility and governorates at ( $p < 0.05$ ).

**Table (4.3): Distribution of male infertility causes by governorate**

Governorates	Unknown cause		Medical cause		Accident		Medication		Total	
	N	%	N	%	N	%	N	%	N	%
Nablus	22	3.5%	62	9.9%	2	0.3%	3	0.5%	89	14.2%
Jenin	22	3.5%	45	7.2%	1	0.2%	0	0%	68	10.8%
Tubas	2	0.3%	12	1.9%	1	0.2%	0	0%	15	2.4%
Salfit	7	1.1%	14	2.2%	0	0%	0	0%	21	3.3%
Qalqilya	6	1.0%	15	2.4%	0	0%	0	0%	21	3.3%
Tulkarm	7	1.1%	27	4.3%	0	0%	1	0.2%	35	5.6%
Ramallah	55	8.8%	62	9.9%	3	0.5%	2	0.3%	122	19.5%
Bethlehem	24	3.8%	18	2.9%	0	0%	1	0.2%	43	6.9%
Hebron	58	9.3%	69	11%	3	0.5%	4	0.6%	134	21.4%
Jerusalem	29	4.6%	32	5.1%	1	0.2%	2	0.3%	64	10.2%
Jericho	5	0.8%	10	1.6%	0	0%	0	0%	15	2.4%
<b>Total</b>	<b>237</b>	<b>37.8%</b>	<b>366</b>	<b>58.4%</b>	<b>11</b>	<b>1.8%</b>	<b>13</b>	<b>2.1%</b>	<b>627</b>	<b>100%</b>

Table 4.4 shows the distribution of male infertility causes among male age groups. In men less than 30 years old, percentages were much higher than other older age groups. Also we noticed that ratios gradually decreased with increasing age groups especially in cases of unknown and medical causes. Fishers exact test showed no significant differences between male infertility causes among male age groups ( $p=0.075$ ).

**Table (4.4): Distribution of male infertility causes by age**

Causes	<30		30-34		35-40		>40	
	N	%	N	%	N	%	N	%
<b>Unknown</b>	75	12.0%	62	9.9%	58	9.3%	42	6.7%
<b>varicocele</b>	91	14.5%	46	7.3%	48	7.7%	18	2.9%
<b>Obstruction</b>	50	8%	26	4.1%	19	3.0%	18	2.9%
<b>Hormonal problems</b>	14	2.2%	4	0.6%	9	1.4%	5	0.8%
<b>Medication</b>	5	0.8%	2	0.3%	5	0.8%	1	0.2%
<b>Spinal cord injury</b>	5	0.8%	2	0.3%	4	0.6%	0	0%
<b>Cryptorchidism</b>	4	0.6%	4	0.6%	2	0.3%	0	0%
<b>Testicular failure</b>	2	0.3%	2	0.3%	2	0.3%	2	0.3%
<b>Total</b>	246	39.2%	148	23.6%	147	23.4%	86	13.7%

Distribution of male infertility causes by occupation in table 4.5 showed that workers, office employees, and business owners had the highest percentages in both unknown and medical causes. While for accidents we found that unemployed had the highest ratios.

**Table (4.5): Distribution of male infertility causes by occupation (2007-2009)**

Occupations	Unknown cause		Medical cause		Accident		Medication	
	N	%	N	%	N	%	N	%
Office employees	56	8.9%	79	21.6%	1	0.2%	3	0.5%
Workers	69	11%	128	20.4%	0	0%	2	0.3%
Teachers	7	1.1%	13	2.1%	0	0%	0	0%
Health professionals	5	0.8%	8	1.3%	0	0%	1	0.2%
Artisans	20	3.2%	28	4.5%	0	0%	1	0.2%
Drivers	20	3.2%	16	2.6%	0	0%	0	0%
Unemployed	220	3.5%	27	4.3%	7	1.1%	3	0.5%
Business owners	27	4.3%	37	5.9%	1	0.2%	3	0.5%
Military employees	9	1.4%	22	3.5%	2	0.3%	0	0%
Farmers	2	1.3%	8	1.3%	0	0%	0	0%

### 4.3 Seminal characteristics

Table 4.6 shows seminal volume, sperm concentration, and total sperm output according to infertility groups. Men with primary infertility had lower seminal characteristics compared to men with secondary infertility.

**Table (4.6): Seminal characteristics by infertility status. <sup>a</sup>**

Seminal characteristics	Primary infertility (n=388) Mean± SD	Secondary infertility (n=82) Mean± SD	p-value	All cases (n=470) Mean± SD
Seminal volume (ml)	3.2±1.67	3.4 ±1.88	0.679	3.3±1.71
Sperm concentration (x 10 <sup>6</sup> /ml)	4.85±5.2	6.1 ±5.4	*0.010	5.07 ±5.3
Sperm output (x 10 <sup>6</sup> )	16.16± 22.0	21.46 ±25.0	*0.011	17.1 ±22.3

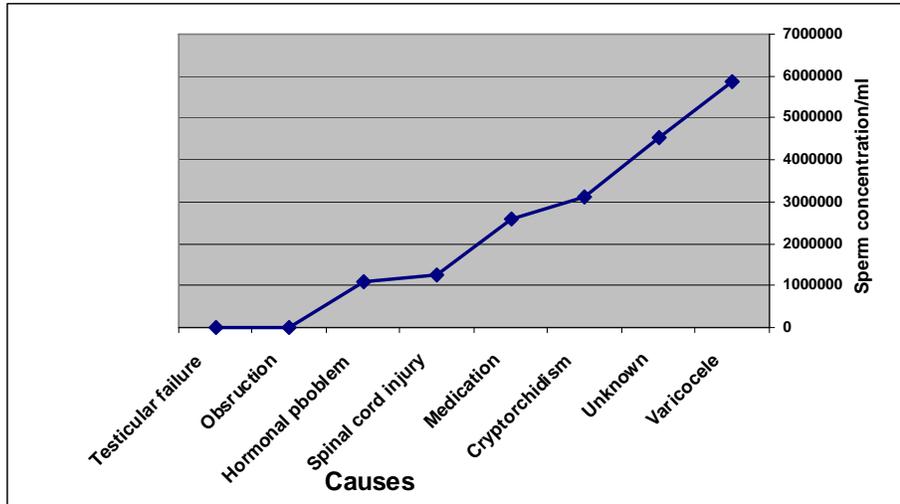
<sup>a</sup>157 men were excluded (127 azoospermic, 9 aspermic, 8 sterile, and 13 cryptospermic)

Note: Analysis was conducted using the Mann-Whitney U test for all variables.

\* statistically significant at p <0.05

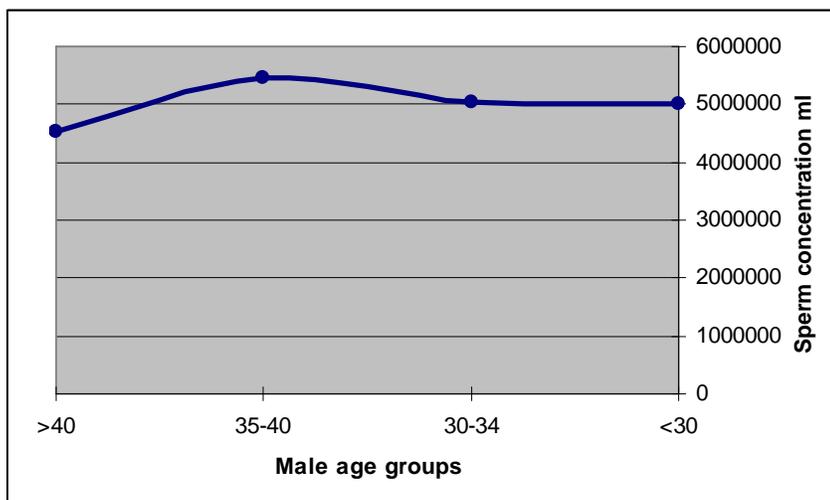
For infertility type, Mann-Whitney test shows a significant difference between type of male infertility and mean of sperm concentration ( $p < 0.05$ ). It was found that males with secondary male infertility had higher sperm concentration than men with primary male infertility. For the type of infertility and sperm output there was also a significant difference ( $p < 0.05$ ) in which males with secondary male infertility had higher sperm output number compared with males with primary male infertility, while between infertility type and semen volume there was no difference ( $p = 0.679$ ).

Figure 4.3 shows the mean of sperm concentration for causes of male infertility. Cases with varicocele had the higher mean of sperm concentration, followed by cases with idiopathic infertility, cases with cryptorchidism, and cases who take medications. Kruskal-Wallis test was used to test the differences between sperm concentration, semen volume, and sperm output and the main causes of male infertility. The test showed significant differences between the semen characteristics and causes of male infertility ( $p < 0.001$ ).



**Figure:(4.3): Mean of sperm concentration according to male causes.**

According to male age group Kruskal-Wallis test shows no significant difference between age groups and any of the seminal characteristics. Figure 4.4 shows the mean of sperm concentration for each age group after excluding 157 infertile men, the sperm concentration mean was nearly converged for all age groups. Men aged between 35-40 had the highest mean of sperm concentration followed by men aged between 30-34, while men over forty had the lowest mean of sperm concentration



**Figure(4.4): Mean of sperm concentration for male age groups (2007-2009)**

157 men were excluded [64 (<30), 33 (30-34), 34 (35-40), 26 (>40)]

There was no significant differences between sperm concentration and all of the following; male occupation ( $p=0.524$ ), type of locality ( $p=0.231$ ), years ( $p=0.418$ ), and governorates ( $p=0.694$ ).

The results of semen analysis were classified according to the reference values of WHO for semen classification by years in table 4.7. Of the 627 semen analysis forms, 206 (32.8%) had single factor abnormalities, while 421 (67.2%) had combined factor anomalies. Overall, 329 (52.5%) had three factors defects oligoasthenoterato-zoospermia, 127 (20.3%) subjects of the study had azoospermia, and 92 (14.7%) of men had multiple factors abnormality oligoastheno/terato-zoospermia. Very few of the cases had oligozoospermia 37 (5.9%), cryptospermia 13 (2.1%), necrospermia 12(1.9%), aspermia 9 (1.4%).

Chi-square test shows a significant relation ( $p<0.05$ ) between semen analysis results and years, in 2008 the percentage of three factors defects and necrospermia were the highest compared with other years. While ratios of oligozoospermia were lower than other years. So 2008 had the worst semen parameters compared with 2007 and 2009.

**Table (4.7): Interpretation of the results of semen analysis according to year.**

Semen classification	2007		2008		2009		Total	
	N	%	N	%	N	%	N	%
<b>Oligozoospermia</b>	15	2.4%	11	1.8%	11	1.8%	37	5.9%
<b>Oligoastheno/terato-zoospermia</b>	22	3.5%	27	4.3%	43	6.9%	92	14.7%
<b>Oligoasthenotera to-zoospermia</b>	100	15.9%	133	21.2%	96	15.3%	329	52.5%
<b>Sterile</b>	5	0.8%	2	0.3%	1	0.2%	8	1.3%
<b>Azoospermia</b>	34	5.4%	43	6.9%	50	8.0%	127	20.3%
<b>Aspermia</b>	1	0.2%	3	0.5%	5	0.8%	9	1.4%
<b>Cryptospermia</b>	6	1.0%	2	0.3%	5	0.8%	13	2.1%
<b>Necrospermia</b>	1	0.2%	7	1.1%	4	0.6%	12	1.9%

From the table above 458 males were oligozoospermic, the degree of oligospermia was mild ( $10 - <20 \times 10^6/\text{ml}$ ) in 22.3%, moderate ( $5-10 \times 10^6/\text{ml}$ ) in 16.4%, severe ( $1 - <5 \times 10^6/\text{ml}$ ) in 33.2%, and extreme ( $<1 \times 10^6/\text{ml}$ ) in about 28.1%. The majority of cases had semen concentration below  $5 \times 10^6/\text{ml}$ .

### Summary

The study results showed that the mean age of infertile men was 33.5 years and the majority of male cases had primary infertility. There were eight main causes for infertility in men. The largest single cause was seminal abnormalities of unknown cause, varicocele was the second largest cause, obstructive azoospermia and hormonal abnormalities were relatively common.

Men with primary male infertility had lower seminal characteristics compared to men with secondary male infertility, and the majority of cases (73.1%) were oligospermic, while 20.3% azoospermic, 2.1% cryptospermic, 1.9% necrospermic, and only 1.3% of cases were sterile.

**Chapter Five**  
**Discussion**

## **Chapter Five**

### **Discussion**

In this chapter the study results will be discussed in term of proportion of male factor among infertile couples; demographic characteristics for infertile groups; male infertility causes and semen parameters. The results will be compared with other global and regional studies.

#### **5.1 Discussion**

Off the 1392 files for couples seeked treatment in Razan centers in Nablus and Ramallah governorates during the study period (2007-2009), we found that male factor alone accounted for more than half of infertility among couples (52%), and contributed with female factor in about 2%. Female factor was identified in only 19% of couples, while the rate of unexplained infertility was 27%. The most common cause diagnosis in the most of the studies was male factor, but in this study it is the highest compared with other studies <sup>[84, 86, 100, 102, 103]</sup>. The reason for the high percentage of male factor among Palestinian couples is that Palestine lies under the Israeli occupation and accordingly, our population lived under continuous stress and exposure permanently to toxins (tear gas) and to radiations emitted from Israeli checkpoints. Furthermore, we have thousands of prisoners in Israel prisons who are exposed to various kinds of torture and psychological stress, all these factors can affect the semen parameters in Palestinian men. During data collection from the cases

medical records the researcher found many cases who were in prisons but not all cases were documented in the records.

In this study, most (83.3%) infertile men had primary infertility and 16.7% had secondary infertility. The Increased number of primary infertility over secondary Seminal characteristics by infertility status infertility indicates that congenital abnormalities or severe impairment of sperm production are more likely to be found. On the other hand, Men with secondary infertility had a better chance for future fertility because varicocele, exposure to certain risk factors, or accidents are the reason beyond decreased fertility among secondary infertile men.

In Northern Nigeria primary infertility (96%) was higher compared with our results (83.3%) and only 4% of cases had secondary male infertility <sup>[85]</sup>. While in Egypt, 70.7% of couples had primary infertility and 29.3% had secondary infertility <sup>[103]</sup>. However, in Thailand primary infertility was lower than our findings (61.8% ) while 35.6% of couples had secondary infertility <sup>[88]</sup>. In Sudan, 62.4% of couples had primary infertility and 37.6% had secondary infertility <sup>[102]</sup>. Other two studies in Tanzania<sup>[83]</sup> and Nigeria<sup>[126]</sup> found that secondary infertility for couples was higher than primary infertility; 62.9%, and 73% respectively.

In this study, among 627 infertile men; 38.3% were from Razan center in Nablus governorate, while 61.7% from Razan center in Ramallah governorate. Ramallah center deals with cases from south and middle West Bank so these percentages would be acceptable, because the population

density in the south are more than in the north since the number of the population in southern districts [Ramallah & Al bireh, Bethlehem, Hebron, Jericho, and Jerusalem] was 1,414,108, while the population number in northern districts [Jenin, Nablus, Tubas, Salfit, Qalqiliya, and Tulkarm] was 936,485 according to the Palestinian Central Bureau of Statistics in 2007<sup>[130]</sup>.

Male cases were from the different governorates of West Bank, but Hebron had the highest percentages in both primary (17.1%) and secondary infertility (4.3%). Because Hebron is the highest in terms of population density compared with the other governorates<sup>[130]</sup>. On the other hand, another explanation is that Hebron is closer to the Dimona nuclear reactor that located at Al-Naqab desert and radiations emitted from the reactor can affect the men fertility in Hebron. Ramallah had the second highest percentages of infertile cases (19.5%) followed by Nablus (14.2%). Even though, the population density in Nablus is higher than in Ramallah, but the cases number were higher in Ramallah. These results couldn't be explained why, therefore, further studies should be focused on place of residence and proximity to pollution sources, exact nature of job and degree of exposure to harmful substances.

The age of infertile groups ranged between 20 to 77 years with mean age of 33.5 years old, it was found that age group less than thirty years old had the highest percentages of infertility (39.2%) and this may due to early marriage when the couples get married at young age and failed to conceive

they seek treatment early even before a year. We found that between the period 2007 to 2009, 72 files of couples were excluded because their infertility duration was less than one year.

Men from primary infertility group were significantly younger than men in secondary infertility group (mean age was 33 versus 37 years) because men from the secondary infertility group already had children at the beginning of their married life (when they are young), but subsequently, they exposed to factors that disrupt their fertility and that may happened later at older age.

The mean duration of male infertility in West Bank was five years, this finding come close to the findings in each of; Bangladesh 4.7 years<sup>[90]</sup>, Mongolia 4.9 years<sup>[86]</sup>, and in Sudan the infertility duration was 5.2 years<sup>[102]</sup>. Couples with a duration of 3 years or less have a better chance of future spontaneous pregnancy, while if the duration of infertility has been longer, this indicates a severe biological problem<sup>[3]</sup>. The mean infertility duration in our study was significantly different between the primary (4.7 years) and secondary (6 years) groups, secondary infertile groups had longer infertility duration and this may be due to the following reasons; primary infertile group seek treatment early (at the beginning of their marriage) because they failed in trying to conceive, while for secondary infertile groups since they already had a pregnancy or children they will not think that a problem has occurred and affected their fertility so they will seek treatment after a long period of trying to conceive.

According to occupation, workers made up the largest group of infertile men, but the exact nature of their work was not reported in the medical files. This group of men may be exposed to a great level of stress as occupational stress negatively correlated with the proportion of normal sperm <sup>[42]</sup>. Because they usually work in jobs that require great efforts, like in industrial and construction jobs, these types of work present with an increase in infertility rates because of greater exposure to stress <sup>[43]</sup> and they were most likely to be exposed to physical and chemical hazards at the work place.

The second largest group is office employees, as they work in offices so their work requires them to sit for long time. A study suggests that sitting for long time increased scrotal temperature and affects sperm quality <sup>[48]</sup>. Drivers accounted for 5.7%, not a large percentage despite that drivers are more susceptible to have fertility problems because of increasing the scrotal temperature during driving due to sitting a long time (more than two hours) <sup>[50]</sup>. Farmers are also more susceptible than others to infertility because of using pesticides and insecticides but in this study their proportion was less than 2%.

In the present study, causes of infertility among men were in agreement with the previous reports, with two exceptions: first the proportion of idiopathic infertility was in the general population ranged between 20-30% <sup>[7]</sup> but in this study it was higher. Second, the proportion of men with obstructive azoospermia was also higher than other studies.

Male infertility in this study was mainly due to idiopathic infertility, which accounted to about 37.6% from all male infertility causes. The large percentages of men with idiopathic infertility were workers, but there was no information about the nature of their working, and their working environment and its effect on their fertility in this study.

Certain environmental, occupational, and lifestyle factors can affect the sperm quality in men with idiopathic infertility. Cases with idiopathic infertility had a mean of sperm concentration less than  $5 \times 10^6$  which is very low. The large percentage of idiopathic infertility was in men less than thirty years old, this age group is the most widely used of modern technology. Modern technology can threaten the men fertility, like using cell phones for long time will reduce the number of live sperm <sup>[67]</sup>, also using laptops for long time <sup>[66]</sup> and adoption of certain styles of clothing (wearing tight undertrousers) <sup>[48,49]</sup> will increase the scrotal temperature and reduce the sperm quality.

Industrialization, environmental pollution, use of chemicals, and exposure to hazardous materials can affect male reproductive health <sup>[75]</sup>. Further more, stress can decreased semen parameters in men <sup>[72,73]</sup>, Palestinian men exposed continuously to different types of stress (political and economic), and so they expected to have poorer semen quality compared with other populations. The effect of war on semen parameters has been reported in a Lebanese study, the only parameter that was lowered during the war was sperm concentration <sup>[70]</sup>. And since our population is

under the Israeli occupation, and we had the highest percentage of male factor among all male infertility studies that mean Israeli occupation has an important role in the large percentages of men with fertility problems.

Varicocele was the second clinical cause in this study which affect 32.4% of men, this percentage is similar to that in Brazil (34.3%)<sup>[82]</sup>. And it is less than the findings in each of the following; Spain (17.9%)<sup>[80]</sup>; Siberia (11.3%)<sup>[75]</sup>; and Kenya (5%)<sup>[81]</sup>. Varicocele is not associated with infertility despite abnormal seminal fluid characteristics<sup>[8]</sup>. In our study, men with varicocele had the highest mean of sperm concentration ( $5.88 \times 10^6$ ) compared with other causes, and it may cause reduced fertility by increased scrotal temperature and leading to decrease semen quality.

Obstruction of the seminal tract was seen in 18% of our cases. This ratio is higher than the results of other studies, in Brazil 10.3% of cases had obstruction<sup>[82]</sup>, 8.4% in Mongolia<sup>[86]</sup>, and in WHO study for 8500 couples it was less than 2%<sup>[7]</sup>. Higher proportion of obstructive azoospermia among infertile men indicates that we have large proportion of congenital defect than other countries which results in obstruction of sperm transport.

Out of the 627 semen analysis reports, 329 had Oligoasthenoteratozoospermia (52.5%) and it was the major combined abnormality factor detected during the study period (2007-2009) while azoospermia 127 (20.3%) was the main single abnormality. In addition, 92 (14.7%) of the cases had oligoastheno/terato-zoospermia, and only 37 (5.9%) of cases had oligozoospermia. These results are closer to results from Spain in which

azoospermia was found in 24%, oligoastheno-zoospermia in 8.4%, oligozoospermia in 6.7%, necrospermia in 5.1%, and cryptospermia in 3% [125]. On the other hand, our findings is not comparable with the finding from Nigeria, and USA of which the most common semen abnormality was in sperm motility [127, 84, 90].

WHO recommends for men with sperm concentration below 5-10 m/ml to be screened for structural abnormalities of sex chromosomes and autosomes [3]. In our study the majority of cases had semen concentration below  $5 \times 10^6$ /ml, the abnormality of chromosomal defects increased with the severity of semen concentration, since 58.4% of the study cases had a medical cause for their infertility so genetic counseling is important especially for couples attending to use assisted reproductive treatment.

## **5.2 Study limitation**

One limitation of this study is that the study population was selected from two infertility centers (Razan centers). Although there are other centers for infertility treatment in the middle and south of West Bank, but because of time constrains and difficulties in accessibility make it difficult to involve all infertility centers in this study.

In addition, all the semen analysis were done in Razan laboratories and therefore, the results of the study can not be considered a representative of the general Palestinian male population. Another limitation is in external validity (extent to which the results of the study apply to people not in the

study) because a convenience sample was used instead of population based random sample.

Another drawback of this study was the design, cross-sectional design can not be used to assess the causality, and in this study we had a large percentage of idiopathic infertility so we could not investigate the causes and factors that contributed to idiopathic infertility by using cross-sectional design. Case-control design are more appropriate in examining the causes and the risk factors associated with male infertility but sensitivity of the study subject and limited time make it difficult to use this design.

Unavailability of some information that can affect the fertility in men like smoking habits, body-mass index, the exact nature of men occupation, exposure to harmful physical and chemical agents, educational level, and abstinence time to all cases led to few number of variables in this study.

Finally, two limitations related to data collection; medical records of Razan centers were sorted by numbers and not according to dates, so the researcher had to review all the files in the archive of the centers and this required a lot of efforts and time. Also during filling the compiled sheets from the files, the researcher faced difficulties in reading some files and in explaining some terms, so she received assistance from one of the doctors working in the center.

## **Summary**

In this study male factor alone constitute for 52% of infertility among couples and this percentage was the highest compared with other national and international studies. Also the ratio of primary male infertility was 83.3% which was higher than other ratios in other countries.

Accordingly to the causes of male infertility, the findings were nearly comparable with the findings in other countries, but the percentage of idiopathic infertility and obstructive azoospermia were higher than other studies.

Oligoasthenoterato-zoospermia was the major combined abnormality factor detected during the study period (2007-2009) while azoospermia was the main single abnormality.

**Chapter six**  
**Conclusions and Recommendations**

## **Chapter six**

### **Conclusions and Recommendations**

This chapter includes the main conclusions and recommendations that obtained from our study results.

#### **6.1 Conclusions**

In conclusion, data from the present study showed that male factor alone accounts for almost half of infertility among couples, so men responsible about more than half of problems of infertility that caused delay in conception while women are generally blamed for that. The proportion of primary male infertility was 83.3% and 16.7% of cases had secondary male infertility, primary infertility was higher in younger men (<30 years), while secondary infertility proportion was higher in men aged between 35 to 40 years old.

Seminal abnormalities of unknown cause (idiopathic infertility) was the largest single cause of male infertility, followed by varicocele, obstructive azoospermia, hormonal problems, spinal cord injury, cryptorchidism, and testicular failure. Males with secondary infertility had higher sperm concentration and sperm out put than men with primary infertility, however the majority of male infertility cases had semen concentration below  $5 \times 10^6/\text{ml}$ .

#### **6.2 Recommendations**

- Genetic counseling for cases with poor semen parameters, especially for couples attended to use assisted reproductive treatments.

- Further studies are suggested to investigate the following:
  1. The effect of varicocele repair on improving fertility in men with varicocele.
  2. The effect of certain risk factors in idiopathic infertile men such as: BMI; smoking habits; types of exercise; using of modern technology; type of clothes; and exposure to harmful physical and chemical agents.
  3. The prevalence of infertility among couples.
  4. Detention and its effect on fertility among Palestinian prisoners.
- Provide education to infertile men by doctors in charge about potential risk factors that may affect fertility and not just provide treatment because simple changes in lifestyle can improve fertility.

### **Summary**

Further studies are needed in Palestine to assess the magnitude of infertility problem in our society since there are no studies available about infertility causes or even for the prevalence of infertility at the national level.

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**Appendix**

**Compilation sheet**

**File number:(            )**

**Date of entry:.....**

**Wife age:..... Husband age:.....**

**Husband occupation:.....**

**District :.....**

**Marriage duration:.....**

**Infertility duration :.....**

**Type of infertility:.....**

**Number of children:.....**

**Cause of infertility:.....**

.....

**Past medical history:.....**

**Semen analysis results:**

**Abstinence days:.....**

**Sperm count:.....**

**Volume:.....**

**Motility :.....**

**Morphology:.....**

جامعة النجاح الوطنية  
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قدمت هذه الأطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في الصحة العامة بكلية الدراسات العليا في جامعة النجاح الوطنية في نابلس، فلسطين.

2011

ب

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الملخص

تهتم الصحة الإنجابية في فلسطين تحديدا بصحة النساء، متجاهلة دور الرجل في هذه العملية بالرغم من أهمية دوره في الإنجاب. تهدف هذه الدراسة بشكل أساسي إلى التعرف إلى الأسباب الرئيسية للعقم عند الرجال في مركزين للعقم في الضفة الغربية.

تضمنت الدراسة 627 ملفا طبيا لجميع الرجال المسجلين في مركز رزان في كل من محافظتي نابلس و رام الله، و الذين يعانون من صعوبة في الإنجاب ما بين عامي 2007 و 2009. لقد تبين من خلال هذه الدراسة أن الزوج كان مسؤولا عن 52% من نسبة العقم بين الأزواج الذين يعانون مشاكل في الإنجاب، و يعاني 627/522 (83.3%) من الرجال من عقم أولي و 627/105 (16.7%) من عقم ثانوي. كان معدل مدة العقم خلال فترة الدراسة  $5 \pm 3.99$  سنوات، و تراوحت أعمار الرجال ما بين 20-77 سنة، بمعدل  $33.5 \pm 7.24$  سنة.

و كان سبب العقم غير المعروف عند النسبة الأكثر من الحالات، هي 37.3%، بينما كان 32.4% من الحالات يعانون من دوالي الخصيتين، و قد وجد أن 18% من الحالات يعانون من انسداد في الجهاز التناسلي، و 5.1% يعانون من مشاكل هرمونية. و تمثلت الأسباب الأقل شيوعا بما يلي: 2.1% من الحالات تتعاطى أدوية تؤثر على الإنجاب، وعند 1.8% من الحالات إصابة في الحبل الشوكي، و 1.6% تأخر في نزول الخصيتين، و 1.3% عندهم فشل في الخصيتين.

ج

و هنا تؤكد الدراسة أن الرجل مسؤول عن أكثر من نصف مشاكل الخصوبة و الإنجاب عند الأزواج، و شكلت نسبة العقم غير المعروف السبب النسبة الكبرى من الأسباب. هذه الدراسة تبين أن فهمنا للدور الإيجابي للرجل و العوامل التي تؤثر فيه غير كاف، و هناك حاجة لإجراء المزيد من الدراسات لبحث أثر العوامل البيئية بالأخص على الحالات التي تعاني من أسباب غير معروفة للعقم في الضفة الغربية.