# SEXUAL DYSFUNCTION AND METABOLIC SYNDROME AMONG DIABETIC MALES VISITING THE TEMA GENERAL HOSPITAL

A THESIS SUBMITTED IN
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School of Medical Sciences

by

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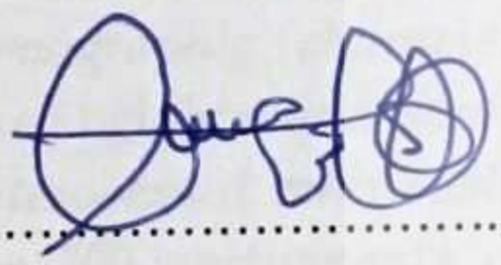
# DECLARATION

The experimental work described in this thesis was carried out at the Department of Molecular Medicine, KNUST and Tema General Hospital, Tema. This work has not been submitted for any other degree.



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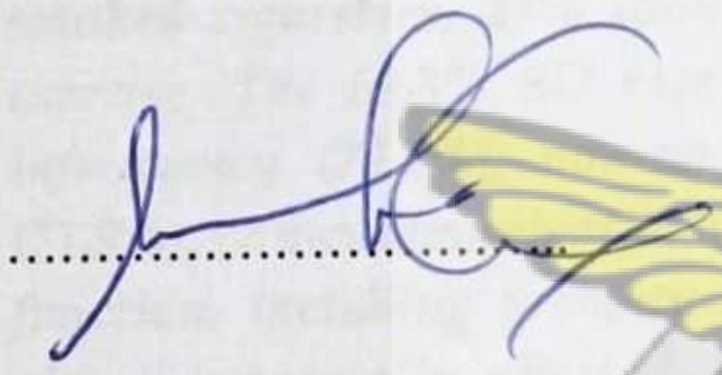

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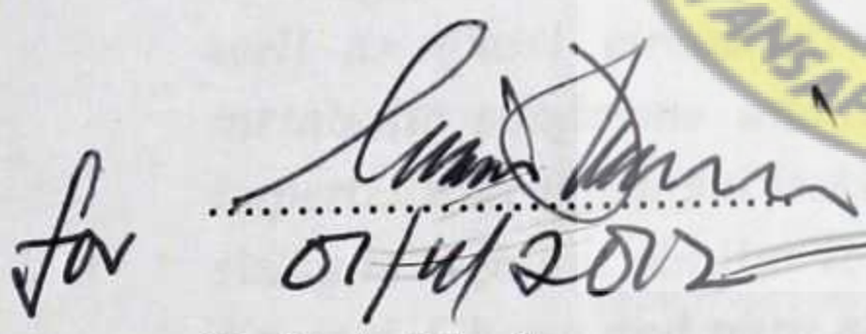

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## ABSTRACT

*Diabetes mellitus is a chronic disease that can result in various medical, psychological, metabolic and sexual dysfunctions (SD) if not properly managed. SD in men is a common under-appreciated complication of diabetes and it is complicated with the development of dyslipidaemia as a result of the metabolic syndrome. This study assessed the prevalence and determinants of SD and metabolic syndrome among diabetic patients in Tema, Greater Accra Region of Ghana. Sexual dysfunction and metabolic syndrome was determined in 274 consecutive diabetic men (age range: 18-82 years) visiting the diabetic clinic of Tema General Hospital between November, 2010 and March, 2011 using the Golombok Rust Inventory of Sexual Satisfaction (GRISS) questionnaire and the WHO, NCEP ATP III and IDF criteria respectively. In addition to the socio-demographic characteristics of the participants, the level of glycosylated haemoglobin and serum testosterone was assessed. All the men had a steady heterosexual relationship for at least 2 years before enrolment in the study. Out the 300 participants contacted, the response rate was 91.3% after 20 declined participation and 6 incomplete data were excluded All the respondents had at least basic education, 97.4% were married, 65.3% were known hypertensive, 3.3% smoked cigarettes, 27% took alcoholic beverages and 32.8% did some form of exercise. The 69.3% SD rate observed in this study appears to be related to infrequency (79.2%), non-sensuality (74.5%), dissatisfaction with sexual acts (71.9%), non-communication (70.8%) and impotence (67.9%). Other areas of sexual function, including premature ejaculation (56.6%) and avoidance (42.7%) were also substantially affected. However, severe SD was seen in only 4.7% of the studied population. The perceived "adequate", "desirable", "too short" and "too long intra-vaginal ejaculatory latency time (IELT) are 5-10, 5-10, 1-2 and 15-30 minutes respectively. Testosterone correlates negatively with glycated haemoglobin (HbA1c), FBG, perceived desirable, too short IELT, and weight as well as waist circumference. There was a positive association of SD with metabolic syndrome and a significant difference in the duration of diabetes, hypertension when subjects were stratified by sexual function. SD rate from this study is high but similar to that reported among self-reported diabetic patients in Kumasi, Ghana and vary according to the condition and age. The determinants of SD from this study are income level, exercise, obesity, higher perception of "desirable" and "too short" IELT. Metabolic syndrome is strongly associated with hypertension, duration of diabetes and testosterone levels.*

# ACKNOWLEDGEMENT

My greatest gratitude goes to the almighty God for seeing me through the programme.

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# ABBREVIATIONS

| | |
|---|---|
| Ach | Acetylcholine |
| ADT | Androgen Deprivation Therapy |
| AV | Avoidance |
| BMI | Body Mass Index |
| cGMP | Cyclic Guanosine Monophosphate |
| CVD | Cardiovascular Disease |
| DIS | Dissatisfaction |
| ED | Erectile Dysfunction |
| EDTA | Ethylene Diamine Tetraacetic Acid |
| eNO(S) | (Endothelial) Nitric Oxide (Synthase) |
| GRISS | Golombok-Rust Inventory for Sexual Satisfaction |
| IELT | Intra-vaginal Ejaculatory Latency Time |
| IMP | Impotence |
| INF | Infrequency |
| IR | Insulin Resistance |
| LH | Luteinizing Hormone |
| MetS | Metabolic syndrome |
| MMAS | Massachusetts Male Aging Study |
| NHANES | National Health and Nutritional Examination Survey |
| NPT | Nocturnal Penile Tumescence |
| NS | Non-sensuality |
| PDEF | Phosphodiesterase 5 |
| PE | Premature Ejaculation |
| QoL | Quality of Life |

| | |
|---|---|
| ROS | Reactive Oxygen Species |
| SD | Sexual Dysfunction |
| SolGC | Soluble Guanylate Cyclase |
| TG | Triglycerides |
| WHO | World Health Organization |



*Chapter 1*

# INTRODUCTION

## 1.1 GENERAL INTRODUCTION

A significant number of men worldwide suffer from some form of sexual dysfunction (SD) ranging from mild to somewhat severe forms. This has serious implications on the quality of life of such individuals as well as their spouses or partners and invariably the whole family. Sex is well known to be a very important measure of the quality of life of an individual and any impairment in sexual function is known to cause dissatisfaction with life in general. Apart from procreation, sex is also seen as a source of enjoyment and a natural relaxant in which affection, care, validation and commitment is exchanged among partners. SD therefore puts a strain on intimacy, affection and invariably the overall quality of life in relationships. The frustrations that result could result in anger, apathy, depression and the loss of self-confidence and self-worth, putting further strain on relationships.

Diabetes has long been established as a risk factor for SD and it is estimated that 35–75% of men with diabetes have SD and this develops 5–10 years earlier (2005). Diabetics are about three to four times more likely to develop SD and are relatively severe and more debilitating than in men without SD. This can be worsened by other comorbid factors such as smoking, hypertension, alcohol, obesity and autonomic neuropathy. Almost 100% of men with diabetic neuropathy will have SD. Erectile dysfunction which is a component of SD was found in the Massachusetts male aging study to affect 52% of men between the ages of 40 and 70 (Feldman *et al.*, 1994), and is expected to double over the next 25 years (Derby *et*

*al.,* 2000). This has serious economic and social implications vis a vis the general increase in life expectancy and the subsequent desire for men to continue to enjoy sex even as they age and are able to manage the threat of diabetes .

Chronic hyperglycaemias as well as dyslipidaemia are the major underlying biochemical factors in diabetes. The contribution of these abnormalities to both macro and micro vascular complications is well known however their contribution to SD is still open to debate. Diabetics are more likely to suffer SD probably because of shared factors impairing hemodynamic mechanisms in both penile and systemic vascular beds.



The metabolic syndrome (MetS) is characterized by a cluster of factors such as hyperglycemia, dyslipidaemias, high blood pressure, obesity and insulin resistance and has long been associated with diabetes. However the extent of interaction and contribution of the individual components to the syndrome is poorly understood. Similarities in aetiology of the MetS with diabetes as well as SD can be traced to endothelial function and it is therefore not surprising that an increased incidence of SD and MetS is largely reported to be among diabetics. The MetS has received attention in recent years because of its association with similar pathophysiologic states such as heart failure (Ingelsson *et al.,* 2006), type 2 diabetes mellitus (Imam *et al.,* 2007), and erectile dysfunction (ED) (Barnas *et al.,* 2005).

Recently, hypogonadism has been thought to be a risk factor for the development of MetS and diabetes (Miner *et al.,* 2007). Patients with higher Testosterone levels have been observed to have lower than 3 components of the MetS. This inverse relationship between MetS components and mean baseline testosterone levels is supported by large body of emerging evidence (Blouin *et al.,* 2005, 2006 ; Kaplan *et al.,* 2006). The recent findings that testosterone modulates NO production as well

as the expression of PDEF5 enzyme has led several researchers into investigating the extent of influence of testosterone levels on SD (Andric *et al.*, 2010).

## 1.2 JUSTIFICATION OF THE STUDY

This study therefore seeks to establish and provide evidence of the relationship between SD, metabolic syndrome, hypogonadism and diabetes. It also seeks to establish and provide evidence regarding the influence and contribution of various risk facors to these conditions and the extent to which such risk factors interplay in the various conditions. The study also seeks to establish the contributions of stereotyped perceptions of intra-vagina ejaculatory latency time (IELT) and the extent to which these perceptions affect sexual functions.

This study will go a long way in helping clinicians and sex therapists in Ghana to appreciate the local situation regarding SD and to understand the dynamics and aetiological factors involved regarding the sexual function of diabetics. It is also invariably going to educate and establish, possibly eradicate, the contribution of higher IELT expectations to SD and thus improve on the quality of life of such persons.

## 1.3 SIGNIFICANCE OF THE STUDY

Over the past 25 years, advances have been made in glycaemic control with insulin delivery (pendevices and CSII with pumps), home blood glucose monitoring, glycated haemoglobin measurements, leading to a reduction in micro-angiopathic complications (retinopathy, nephropathy and neuropathy). Better glycaemic control along with the use of statins and renin-angiotensin blocking agents as part of aggressive blood pressure reduction have resulted in improvements in

macroangiopathic complications (cardiovascular, cerebrovascular and peripheral vascular disease). How have these interventions reduced the frequency and relationship between SD and MetS over the past two–three decades.

It is hoped that information provided in this study will help scientists and healthcare policy makers to develop appropriate and timely strategies to meet current and future demands to prevent and/or alleviate male sexual dysfunction in Ghana.

- It is also hoped that material provided in this study will help the reproductive endocrinologist to widen the scope of his or her professional activity from the limited focus on gonadal function to the wider consideration of all inseparable and integrated aspects of human sexual and reproductive capacities.



## 1.4 AIM OF THE STUDY

The aim of this study was to assess SD and metabolic syndrome among diabetic patients visiting Tema General Hospital.

## 1.5 SPECIFIC OBJECTIVES

- To assess the prevalence of SD in diabetic patients
- To assess the prevalence of MetS in diabetic patients using WHO, ATP III and IDF criteria
- To assess the association between SD, MetS and hypogonadism among these patients.
- To determine the risk factors for SD and MetS

# *Chapter 2*

# LITERATURE REVIEW

## 2.1 BACKGROUND

One of the main aims of marriage is for procreation (reproduction) and more importantly for sexual and emotional fulfillment for both partners. Reproduction is however preceded by the mating process which is often called sexual intercourse which provides the platform for an egg and a sperm to fuse into fertilization. Sexual fulfillment is achieved via the sex organs, (vagina and penis). The inability of these organs and processes involved to function normally is termed sexual dysfunction (Guay *et al.*, 2003b).



## 2.2 MALE SEXUAL FUNCTION

Sexuality is a complex process, multidimensional phenomenon that incorporates biological, psychological, interpersonal and behavioral dimensions. In a research by Kolodny *et al.*, (2003), it was revealed that the psycosexual response cycle consists of four phases: excitement, plateau, orgasm and resolution phases (Kolodny, 2003). Several other classifications of the sexual cycle have basically sought to classify the same processes with emphasis on the functional activities with the inclusion of the sex seeking behavior as part of the process, thus the normal male sexual response cycle is divided into five interrelated events that occur in a defined sequence: libido, erection, ejaculation, orgasm and detumescence.

### *2.2.1 Libido or sexual desire*

Libido is defined as the biological need for sexual activity (sex drive) and frequently expressed as a sex-seeking behavior. Its intensity is variable between individuals as well as within an individual over a period of time. Higher serum testosterone levels appear to be associated with this greater sexual activity in healthier older but not younger men (Toone *et al.*, 1983).

### *2.2.2 Erection*

Erection is the enlarged and rigid state of the sexually aroused penis sufficient enough for vaginal penetration. Erection is the final reaction to various psychogenic and sensory stimuli from imaginative, visual, auditory, olfactory, gustatory, tactile, and genital reflexogenic sources, which affect several neurological and vascular cascades that lead to penile tumescence and firmness adequate for vaginal intromission (Kandeel *et al.*, 2001). Erection is also linked with considerable psychological and physical changes, together with increased sexual arousal, full testicular assent and swelling, dilatation of the urethral bulb, enlargement of glans and coronal size, cutaneous flush over the epigastrium, chest, and buttocks, nipple erection, tachycardia and increase in blood pressure, hyperventilation, and widespread myotonia (Kolodny, 2003).



Recent studies suggest that gonadal androgens tone penile erection via local control of NO secretion and/or activity (Kandeel *et al.*, 2001). The control of the frequency of non erotic or "reflex" erection due to androgen, proposes a possible role for peripheral androgen activities in the human (Davidson *et al.*, 1982). Because androgens can improve Nocturnal Penile Tumiscence, (NPT) and not erection in reaction to erotic stimuli (Davidson *et al.*, 1982). This implies that sexual behavior and erection are androgen dependent and acting both centrally and peripherally (Heaton and Morales, 2003).

### *2.2.3 Ejaculation*

Ejaculation is the act of ejecting semen. It is a reflex action that occurs as a result of sexual stimulation. It is made up of two sequential processes, the first called emission is associated with deposition of seminal fluid into the posterior urethra. Simultaneous contraction of the ampulla of the vas deferens, the seminal vesicles and the smooth muscle of the prostate mediate emission (Wagner, 1981). The second phase is the true ejaculation and it is the expulsion of the seminal fluid from the posterior urethra through the penile meatus.

### *2.2.4 Orgasm*

This is the climax of sexual excitement. The entire process of emission and ejaculation is known as the male orgasm (Guyton *et al.*, 2007). Physiologic and psychogenic factors have been found to contribute to the genesis of the orgasmic phase (Hartmann, 1998; Donatucci *et al.*, 2004; Barnas *et al.*, 2005). The following physiological events are the effects of afferent stimuli from the pudendal nerve: smooth muscle contraction of the accomplice sex organs; upsurge and discharge of pressure in the posterior urethra; feeling of the ejaculatory unavoidability; contraction of the urethral bulb and perineum; periodic contractions of the pelvic floor muscles; semen emission and ejaculation; and lastly, the reversal of the generalized physiological changes and sexual tension. These actions are recognized by sensory cortical neurons as enjoyable.

Orgasmic pleasure could be influenced by the degree of sexual pleasure, recency of sexual activity, and the psychosexual composition of the human being. In the absence of the two phases of erection and ejaculation, orgasm can still be achieved. On the other hand, contractions of pelvic musculature and ejaculation could take place in the absence of orgasmic sensations (Kandeel *et al.*, 2001).

### *2.2.5 Detumescence*

This is the phase where the penis returns to the flaccid state due to vasoconstriction of the arterioles and return of events inside the contractile corporeal units reroute the blood away from the cavernous sinuses and allow a rise in the venous evacuation of their contents (Kandeel *et al.*, 2001). At first, the rate of blood seeping away rises by about 10-fold, followed by a gradual fall until it gets to the pretumescence level (Priviero *et al.*, 2007) and a period of inhibition to the recommencement of erectile and ejaculatory functions. The duration of this refractory phase is reliant upon many factors including age, physical state, and psychological environment (Carrier *et al.*, 1993).



## 2.3 ANATOMY AND PHYSIOLOGY OF PENILE ERECTION

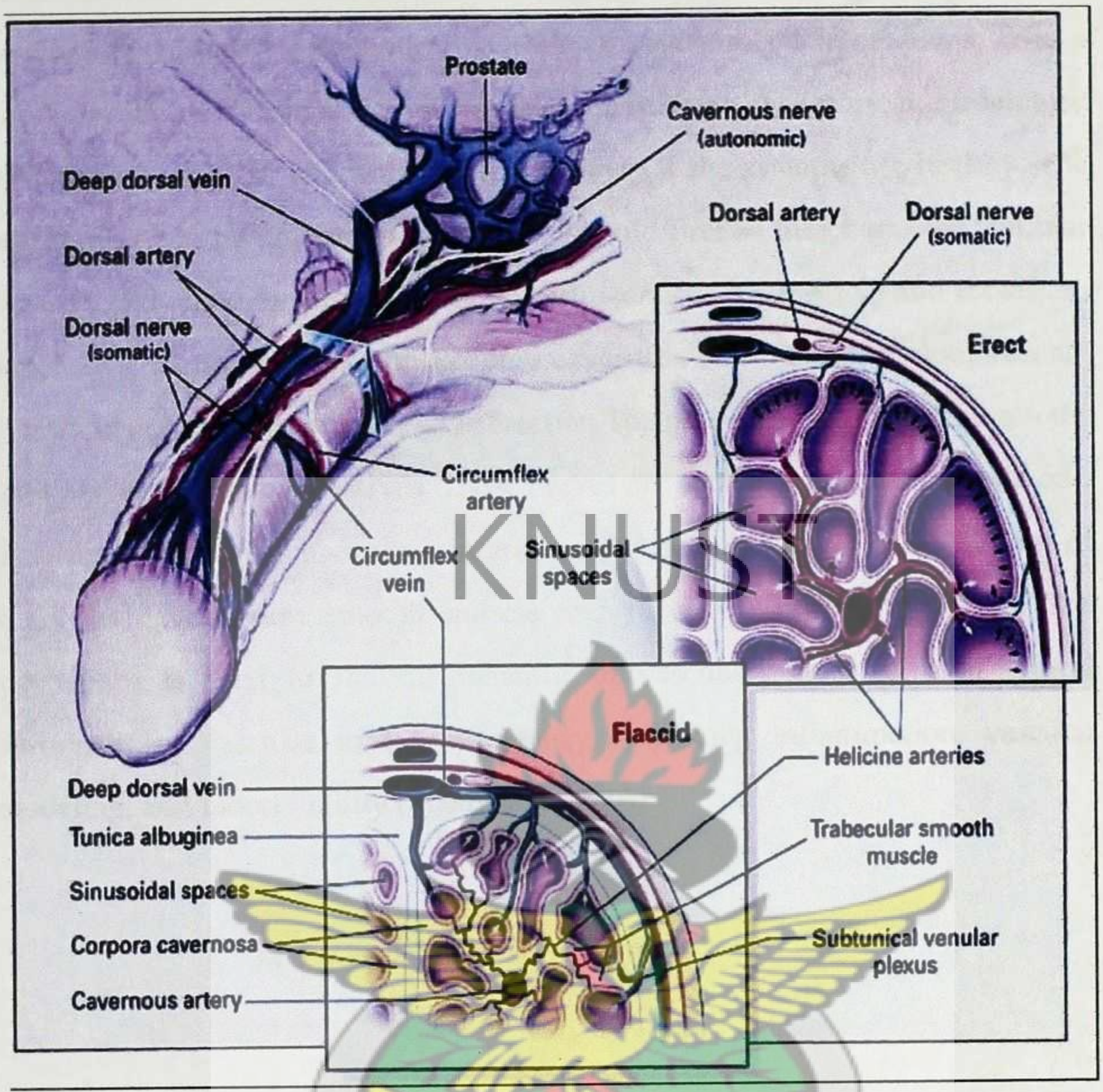


**Figure 2.1** Mechanism of Penile erection and flaccidity.

**The corpora cavernosa and corpus spongiosum received cavernous nerves (autonomic) to control penile blood flow for the period of erection and detumescence. Pudendal nerves branches; dorsal nerves (somatic) are principally responsible for penile sensation. During erection (upper right), relaxation of the trabecular smooth muscle and vasodilatation of the arterioles leads to a number of increases in blood flow, this expands the sinusoidal spaces to elongate and expand the penis. This expansion compresses the subtunical venular plexus against the tunica albuginea. Apart from that, stretching of the tunica compresses the outlet veins, in consequence reducing the outpouring of blood to a minimum. In the flaccid state (lower right), inflow via the constricted and twisted helicine arteries is limited, leading to free outflow through the subtunical venular plexus (Lue, 2000a).**

The creation and maintenance of erectile function involves series of hormonal, neurological, vascular, biochemical as well as psychosocial interactions. It is a complex process that reflects a dynamic balance between excitatory and inhibitory mechanisms and these will only work effectively if the systems are healthy. The integrity of the hypothalamic pituitary axis should first be intact and the vascular system should allow for proper vascular perfusion for any effective and consistent erection. The corpus spongiosum, corpora cavernosa and the tunica albuginea are the main structures involved in penile erection.The nerves serving the penis are the dorsal penile and perineal nerves. These nerves are a continuation of sympathetic, parasympathetic, and sensory and motor somatic nerves. They control the tone of the corpus cavernosum smooth muscle and its related vascular system. The endothelium is vital to the maintenance of vascular health. It is a critical determinant of vascular tone and patency, reactivity, inflammation, vascular remodeling, and blood fluidity (Thethi *et al.*, 2005).

## 2.4 MECHANISM OF ERECTION

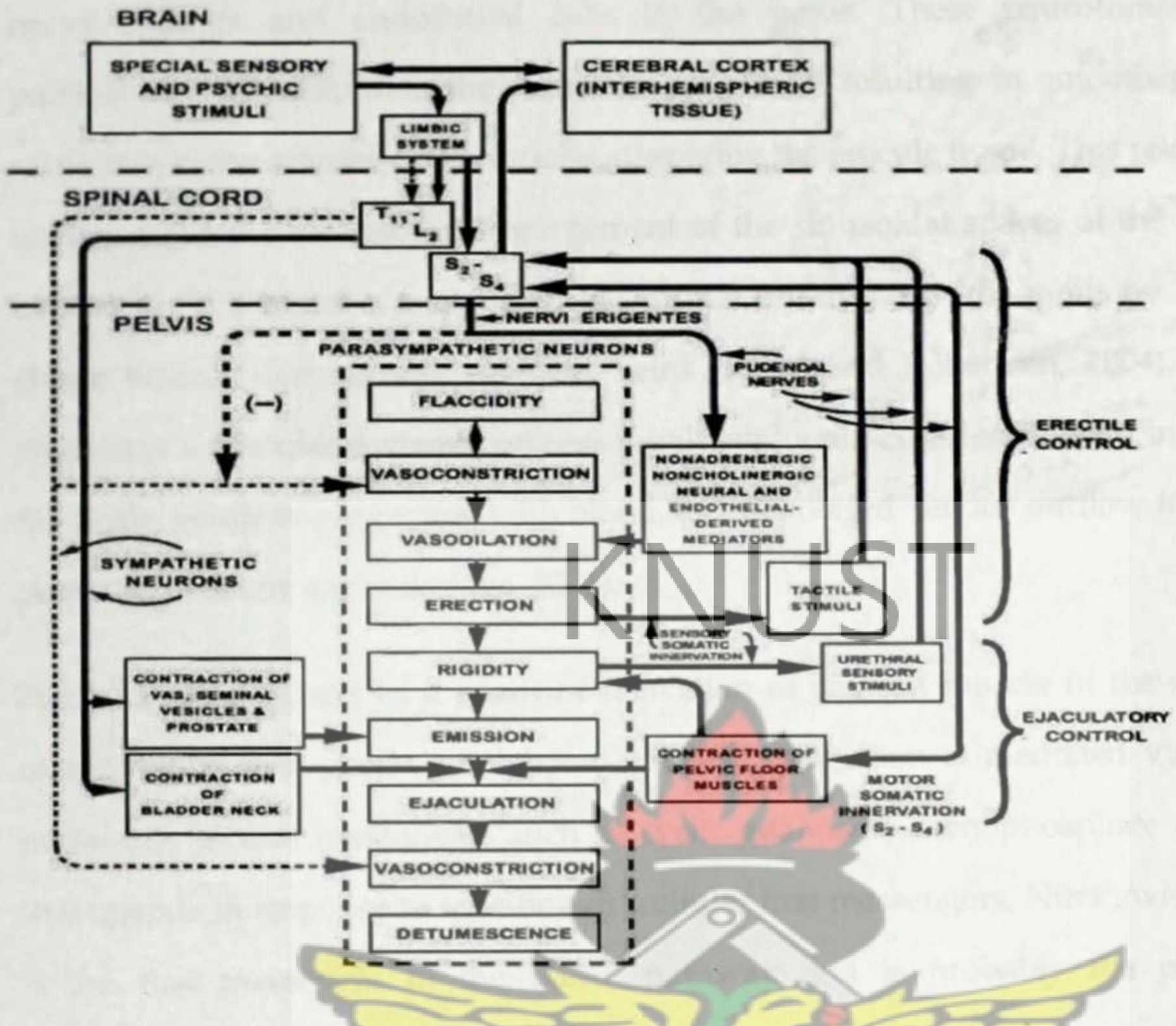


**Figure 2.2** Control of male sexual cycle.

**Connections of autonomic and somatic innervations. Pudendal nerve carried the sensory input from the genital tract to the S2–S4 section of the spinal cord. Ascending sensory fibers synapse in the corticomedullary junction and the thalamus, and then terminate in the contralateral principal sensory area deep in the interhemispheric tissue. Somatic motor fibers start off from the sacral segments S2–S4 and furnish the pelvic floor muscles and the external anal sphincter. Descending parasympathetic innervation leaves spinal cord at the S2–S4 level and get to the penis through pelvic nerve and liable for corporeal vasodilatation and corporeal smooth muscle relaxation. These lead to penile change from the flaccid to the erect state. Penile erection stimuli getting to the spinal cord through pudendal nerve produced more reflex arcs to help set off and/or keep the erection. Sympathetic innervation exits the spinal cord at T11–L2 level, getting to the penis through the lower mesenteric, hypogastric, and pelvic plexuses. Through coordinated contractions of the vas deferens, ampulla, seminal vesicles, prostate, and the bladder neck, it is in charge of emission and ejaculation. Somatic innervation-mediated contraction of the pelvic floor muscles helps in attaining maximum penile firmness with releasing the ejaculatory fluid. Sympathetic innervation mediates corporeal vasoconstriction and corporeal smooth muscle contraction, and thus causes penile detumescence after the orgasmic relief. Activation of one division of autonomous system is associated with inhibition of the other (Litwin *et al.*, 1998).**

Arousal generates nerve impulses that cause the release of neurotransmitters from nerve endings and endothelial cells in the penis. These neurotransmitters particularly NO, stimulate the formation of cGMP resulting in smooth muscle relaxation in the arteries and arterioles supplying the erectile tissue. This relaxation increases blood flow causing engorgement of the sinusoidal spaces of the corpus cavernosa. The blood is trapped in the corpus cavernosa of the penis by fibrous elastic tunicae that occlude draining veins (Hood and Robertson, 2004). Penile erection is a vascular dynamic process involving increased arterial blood inflow to the penis, penile engorgement with blood, and decreased venous outflow from the penis (Stanislavov and Nikolova, 2003).



Penile erection occurs as a result of relaxation of smooth muscle in the corpora cavernosa. Within penile smooth muscle cells, relaxation is mediated via cyclic nucleotide second messengers such as cyclic guanosine monophosphate (cGMP) that operate in response to specific extracellular first messengers. Nitric oxide (NO) is the first messenger in the cGMP pathway and is probably the principal neurotransmitter mediating tumescence. It is released by non-drenergic, non-cholinergic nerves in response to sexual stimulation and by the endothelium of the corpus cavernosum in response to the sheer stress of blood flow in the presence of acetylcholine. When cGMP causes relaxation of cavernosal smooth muscle, the inflow of blood into the penis is faster than its venous outflow and the result is penile rigidity (Snow *et al.*, 2002). The more blood that flows in, the longer this inflow is maintained, and the longer the outflow is prevented, the longer an erection will be sustained. The metabolic breakdown of pro-erectile cGMP by phosphodiesterase enzymes eventually leads to detumescence.

Pudendal nerve carried the sensory input from the genital tract to the S2–S4 section of the spinal cord. Ascending sensory fibers synapse in the corticomedullary junction and the thalamus, and then terminate in the contralateral principal

sensory area deep in the interhemispheric tissue. Somatic motor fibers start off from the sacral segments S2–S4 and furnish the pelvic floor muscles and the external anal sphincter. Descending parasympathetic innervation leaves spinal cord at the S2–S4 level and get to the penis through pelvic nerve and liable for corporeal vasodilatation and corporeal smooth muscle relaxation. These lead to penile change from the flaccid to the erect state. Penile erection stimuli getting to the spinal cord through pudendal nerve produced more reflex arcs to help set off and/or keep the erection. Sympathetic innervation exits the spinal cord at T11–L2 level, getting to the penis through the lower mesenteric, hypogastric and pelvic plexuses. Through coordinated contractions of the vas deferens, ampulla, seminal vesicles, prostate and the bladder neck, it is in charge of emission and ejaculation. Somatic innervation-mediated contraction of the pelvic floor muscles helps in attaining maximum penile firmness with releasing the ejaculatory fluid. Sympathetic innervation mediates corporeal vasoconstriction and corporeal smooth muscle contraction and thus causes penile detumescence after the orgasmic relief. Activation of one division of autonomous system is associated with inhibition of the other (Litwin *et al.*, 1998).

Two neurotransmitters that are significant in the erectile process are dopamine and serotonin. These neurotransmitters influence the male sex drive. Dopamine is the chemical messenger that relays pleasure, while serotonin tells the body to be calm. Dopamine can send positive signals to the brain to encourage sexual activity, while low dopamine levels will decrease libido. Low levels of serotonin can affect our mood and aggression levels also decreasing libido (Lamm, 2005).

## 2.5 MALE SEXUAL DYFUNCTION

The WHO defines SD as "the various ways in which an individual is unable to participate in a sexual relationship as he or she would wish". Most SD has been thought of as being psychogenic in its aetiology but recent evidence has corrected that perception and established that the large majority of SD is caused by organic causes and exacerbated by metabolic risk factors. The effect of impaired sexual function could be mild, moderate or severe with each category having different outcomes for treatment and restoration of normalcy. SD in men can manifest in different forms such as impotence, premature ejaculation, non-sensuality, avoidance, dissatisfaction, non-communication and infrequency. ED (impotence) is the main cause of SD in men and it has been thought to be the primary cause that eventually manifests itself into the other forms of SD. ED is defined as the inability to achieve and maintain an erection sufficient for satisfactory sexual performance.

Sexuality and sexual behavior are shaped by the interaction of psychological, social and biological factors specific for each individual. Problems arising in one or more of these areas may affect sexual functioning in the male or the female. Family and marital therapists are usually inclined to see the sexual dysfunction as a symptom resulting from disrupted relations between spouses, ignoring other areas. While sex therapists tend to focus only on the sexual dysfunction in the therapeutic context. The communication and intimacy between spouses, exchange in feelings and thoughts are usually overlooked by therapists coming from a variety of disciplines (Işıklı, 1993).

### *2.5.1 Disorders of libido/desire*

Disorders of desire or decreased libido are characterized by lack or absence of sexual desire or sexual fantasies for some period of time. The condition ranges from a general lack of sexual desire to lack of sexual desire for the current partner.

This condition may have started after a period of normal sexual functioning or the person may always have had no or low sexual desire (Coretti and Baldi, 2007).

### 2.5.2 *Hypoactive sexual desire (HSD)*

This is defined as persistent or recurrently deficient sexual fantasy and desire for sexual activity leading to marked distress or interpersonal difficulty. Psychosocial causes that can cause this condition include forms of sexual trauma such as incest, rape or sexual abuse. Relational factors that can also cause this include mistrust, conflict, fatigue or stress. (Boehringer I., 2010)



### 2.5.3 *Compulsive sexual behavior (CSB)*

This constitutes all forms of sexual behavior that have strikingly repetitive, compelling or driven qualities. They usually manifest as obsessive, addictive, excessive sex seeking behaviors and associated with depressive disorders and sexual impulsivity.

### 2.5.4 *Disorders of orgasm*

Male orgasmic disorder is defined as persistent or recurrent delay in or absence of orgasm after a normal sexual excitement phase during sexual activity (APA, 1994). Sexual behavior surveys have estimated that approximately 8% of men experience orgasmic difficulties, making male orgasmic disorder the least common sexual disorder in men (Laumann *et al.*, 1999).

### 2.5.5 *Disorders of ejaculation*

There exists a spectrum of disorders of ejaculation ranging from mild premature to severely retarded or totally absent ejaculation, these include premature ejaculation, painful ejaculation, inhibited or retarded ejaculation and retrograde ejaculation.

#### 2.5.5.1 *Premature ejaculation*

This is the most common ejaculatory disorder in men and it is defined as persistent or recurrent ejaculation with minimal sexual stimulation that occurs before, upon, or shortly after penetration and before the person wishes it resulting in distress

and interpersonal difficulty. Some individuals perceive to have premature ejaculation when in actual fact their IELT is normal. This has recently been referred to as premature-like ejaculatory dysfunction.

### 2.5.5.2 *Painful ejaculation*

This type of ejaculatory disorder results from side effects of tricyclic antidepressants. It is a persistent, recurrent pain in the genitals during ejaculation or immediately afterwards.

### 2.5.5.3 *Inhibited or retarded ejaculation*

This is when ejaculation does not occur at all, this occurs in about 3% of men (Kaplan, 1974)



### 2.5.5.4 *Retrograde ejaculation*

This is when ejaculation is forced back into the bladder rather than through the urethra and out of the end of the penis at orgasm.

### 2.5.6 *Failure of detumescence*

Local penile $\alpha$-adrenergic receptor activation is the most important neuromediator effecting detumescence. Interference with this function through the $\alpha$-1 receptor blockade may lead to the development of priapism (Horowitz and Goble, 1979). This results in a prolonged painful erection lasting four or more hours. It can be a primary idiopathic origin or caused by a diseased condition such as leukaemia, sickle cell as well as drugs such as cocaine and other vasoactive injections.

## 2.6 PREVALENCE OF MALE SEXUAL DYSFUNCTION

In the last two decades it has been recognized that endothelial dysfunction and vascular disease are the main causes of erectile problems. Large bodies of evidence have showed a very strong association of cardiovascular risk factors and ED. It is therefore not surprising that various data from several studies have reported

higher proportions of ED amongst diabetics. ED also occurs at an earlier age in diabetic population as compared to the general population and this often related to the duration and the severity of diabetes (Klein *et al.*, 1996; Fedele *et al.*, 1998). The main aetiology in the development of diabetes as well as ED is via impairments in endothelial function, also diabetes is associated with accelerated large vessel atherosclerosis, microvascular arterial disease, autonomic neuropathy, dyslipidaemias, concomitant hypertension and prominent endothelial dysfunction. All of these conditions also contribute to erectile dysfunction (Thethi *et al.*, 2005).

The worldwide incidence of ED is estimated at over 152 million men with a forecast of 322 million men by the year 2025 (Moreland *et al.*, 2001). The largest projection increases is in the developing world that is Africa, Asia, and South America. Africa is projected to have the highest percentage increase of 169% from 1995 to 2025 (Ayta *et al.*, 1999). The National Health and Social Life Survey reports showed that African-Americans are 20% more likely to suffer from erectile dysfunction than Caucasians (Laumann *et al.*, 1999).

Epidemiological studies have increasingly supported the already large body of evidence which shows that diabetic men are three to four times more likely to develop ED as non diabetics. This is supported by the fact that the various risk factors for the development of diabetes are also risk factors for the development of ED. Risk factors such as ageing, obesity, hypogonadism, neurological diseases and hypertension have increasingly been associated with both diabetes and ED. It is estimated that between 35-75% of diabetics have erectile dysfunction and this develops 5-10 years earlier. In the Massachusetts aging male survey ED was reported in 1.1% of men aged 21-30, 55% of men aged 50-60 and 75% of men above 60years. This data suggests the stronger influence of age on both erectile function and diabetes and this is a well documented and established finding.

Jamieson *et al.,* (2008) in a survey of 142 men 40-59yrs with type 1 diabetes reported 54% had ED, with duration of diabetes, age, glycaemic control (HbA1c), weight, hypertension and microalbuminuria being the significant predictors of ED. They observed that those with ED were older by four years on average, had poorer glycaemic control, were heavier by an average of 4kgs and had a higher cardiovascular risk score.

De Berardis *et al.,* (2002) in their study of 1,460 type 2 diabetic patients at an outpatient's clinic in Italy found 37% had frequent ED, 24% reported occasional ED and 42% reported no ED. They observed age, duration of diabetes, worse metabolic control, history of smoking, treatment of diabetes, presence and severity of diabetic complications to be the strongest predictors of ED. They also observed that patients with ED had lower scores of Quality of life, QoL. 45.6% of patients who had frequent ED had severe depressive symptoms. Siu *et al.,* (2001) studied 500 Chinese diabetic men (of which 97% had type 2 disease) at a single medical clinic in Hong Kong in 2001 and found the overall prevalence of ED to be 63.6%.

Amidu *et al.,* (2010b) in a study of 150 ghanaian men with various medical conditions attending an outpatients clinic found 70% of self-reported diabetics had SD and 59.8% among all respondents in the study had SD. (Amidu *et al.,* 2010a) however reported an SD rate of 65.9 % among healthy ghanaian populace in the Kumasi metropolis.

In the Massachusetts Male Aging Study (MMAS) by Feldman *et al.,* (2000), men aged 40-70 years were interviewed in 1987-1989 and reinterviewed in 1995-1997. Data were collected and blood was drawn in participants' homes. ED was assessed from responses to a privately self administered questionnaire. Analysis was restricted to 513 men with no ED at baseline and no diabetes, heart disease or related medications at either time. They found the combined prevalence of minimal, moderate and complete impotence was 52%. The prevalence of complete

impotence tripled from 5 to 15% between subject ages 40 and 70 years. Of the 52% of men who suffer from erectile dysfunction 17% had minimal ED, 25% had moderate ED and 10% had complete ED (Feldman *et al.,* 1994). Nicolosi *et al.,* (2002) reported in their international survey of older adults that the level of satisfaction with present sexual ability was lower in diabetic than non-diabetic subjects and there was a 16% decline in satisfaction amongst diabetic compared to non-diabetic subjects. Diabetic men were more likely to report concern about their ability to have intercourse, whilst the level of concern was similar in diabetic and non-diabetic women.



In their study of sexual dysfunction among type 1 diabetics, Enzlin et al., (2003) found the prevalence of Sexual dysfunction to be 22% in men and 27% in women. BMI, age, duration of diabetes and diabetic complications were the significant predictors of SD in men whilst in women depression and quality of partner relationship had strong correlation with SD. They however found no correlation between SD and HbA1c in both sexes. They therefore suggested that in diabetic men SD was more likely related to somatic and psychological factors whilst in women psychological factors were more prominent.

ED is the resultant inability to achieve and maintain an erection, it is the combination of impairments in possibly some or a few steps responsible for the production of penile erection. This impairment could either be related to the hypogonadal-pituitary axis, gonadal functions or the penile anatomy itself .For the erectile process to function correctly, several systems of the body need to be healthy – blood needs to be flowing smoothly and unobstructed throughout the body, nerves need to be firing and sending messages between the brain and the tissues, and libido needs to be present encouraging sexual interest.

The etiology of ED however involves multiple organic and psychogenic factors that often coexist. Being the most common causes of intermittent erectile malfunction in younger populations, psychogenic factors are usually secondary to or they may coexist with organic factors in older populations (Melman and Gingell, 1999).

Fedele *et al.,* (2000), in their study of 1383 type 1 and 8373 type 2 diabetic men between the ages 20- 69 in 178 diabetic centres in Italy observed ED increased with age for both groups and that type 2 diabetics tend to report ED less frequently than type 1 diabetics. They also observed a positive relationship between ED and poor metabolic control as well as smoking and duration of diabetes for both types. BMI however was observed to be a risk factor only in type 1 diabetes. They measured an ED prevalence rate of 26% in type 1 and 37% in type 2. They also observed that diabetes related arterial, renal, retinal diseases and neuropathy was associated with increased risk of ED in both groups but the OR was higher in the type 1 diabetics. They however observed no relation between alcohol consumption and ED in either group. Bacon *et al.,* (2002), in their large cohort study of 31,027 men aged 53-90 years estimated an ED prevalence of 45.8% for diabetics and 24.1% for non diabetics .They observed that diabetic men had higher relative risk (RR) for having ED than non diabetic men and that men with type 1 diabetes were more likely to have ED than men with type 2 diabetes. They found duration of diabetes to be positively associated with increased risk of ED despite presence of other comorbid factors. They however conceded they might have underestimated the prevalence because diabetic men could have been more likely not to report to the ED outcome questionnaire posted to them.

Such limitations in the methodology as well as several other difference in methodology such as method of sampling, period of sampling, duration of sampling, number of subjects recruited, different methods and definitions used to

measure ED and the specific population and type of diabetics sampled account for the various variations in prevalence estimates as well as differences in observation of certain risk factors. However a large degree of agreements in research has been established and a large body of evidence which will adjust for all the differences could help in establishing concrete understanding of estimates and risk factors, whether sociocultural, biochemical or genetic influences.

Kalter-Leibovici *et al.*, (2005), in their research of 1,040 diabetics attending 26 different diabetic clinics in Israel reported a prevalence rate of severe erectile function of 30.1%. They observed age, duration of diabetes, HbA1c levels, micro vascular disease, cardiovascular disease and diuretic treatment to be significantly associated with ED. They however found consumption of small amounts of alcohol and work or leisure related physical activity to be protective factors. This is interesting as the definition of severe erectile dysfunction is dependent on the methodology used to assess erectile function, it is also obvious that moderate and mild ED which is assessed in many other studies was not reported as ED. Thus the prevalence would have been far higher if these were part of the estimation.

Goldmeier *et al.*, (1998), in their study of 203 heterosexual subjects at a genitourinary medicine clinic in London reported that 24% of men and 12% of women attending clinic for the first time have SD, they observed that 42% of men were diagnosed with erectile dysfunction, 18% dissatisfaction, 13% premature ejaculation, 11% retarded ejaculation, 8% decreased sexual desire, and 16% other problems. Thomas *et al.*, (2005), in their study of 1,078 recruited patients aged 30 to 70 years, 24.5% reporting ED were generally older and the prevalence rose significantly with age, increasing from 6.8 in those aged 30–39 to 35.8% in those 70 years. They also observed that ED patients had worse glycemic control even though more ED patients underwent glucose-lowering treatment and that systolic blood pressure was higher in the ED patients, although 1.7 times more ED patients

were receiving blood pressure–lowering pharmacotherapy. In univariate analysis, they observed hyperglycemia and hypertension increased the risk for having ED but not after adjustment for age and diabetic duration. ED patients had worse renal function and increased levels of micro- and most macrovascular.

The corpora cavernosa and corpus spongiosum received cavernous nerves (autonomic) to control penile blood flow for the period of erection and detumescence. Pudendal nerves branches; dorsal nerves (somatic) are principally responsible for penile sensation. During erection (upper right), relaxation of the trabecular smooth muscle and vasodilatation of the arterioles leads to a number of increases in blood flow, this expands the sinusoidal spaces to elongate and expand the penis. This expansion compresses the subtunical venular plexus against the tunica albuginea. Apart from that, stretching of the tunica compresses the outlet veins, in consequence reducing the outpouring of blood to a minimum. In the flaccid state (lower right), inflow via the constricted and twisted helicine arteries is limited, leading to free outflow through the subtunical venular plexus (Lue, 2000b).

A number of data have recognized some relationship between sexual dysfunction and psychological disorders. In the Massachusetts Male Aging Study, male erectile dysfunction was established to be linked with depressive symptoms. The organic causes of erectile dysfunction can be classified into systemic diseases, endocrine, neurological, vascular, or local penile disorders (Burnett, 2006; Kloner, 2007).

There are several factors involved in ED. ED may be due to psychological, neurological, metabolic, vascular, hormonal or drug related causes. Psychological causes may include stress, anxiety, depression or even expectations. Neurological diseases may include Parkinson's, Alzheimer's disease, diabetic neuropathy, peripheral neuropathy and spinal bifida. Metabolic complications may include hyperlipidemia, diabetes, hypertension, dyslipidaemias, metabolic syndrome.

Vascular causes may include atherosclerosis, vascular injury etc. Approximately 30% of ED is due to the existence of systemic disease which affects the blood delivery to the penis (Feldman *et al.*, 1994). Artherosclerosis, endothelial dysfunction and vascular injury are possible mechanisms that could reduce adequate perfusion. Even though endocrine disorders have been claimed not to be a cause of ED, low testosterone levels have been linked with > 15% of patients complaining of erectile failure (Govier *et al.*, 1996), and hyperprolactinaemia has been shown to be the cause of ED in 2–3% of men presenting with sexual dysfunction (Baskin, 1989). Neurogenic impotence is not unusual (3–10%) and is observed concomitant with multiple sclerosis, discopathies of lumbosacral tract, after prostatectomy and following spinal cord, pelvic, perineal or penile traumas (Berger, 1993).



Psychological causes are frequent (30–40%) and include interactive–experiential problems (depressive– anxious behavior, religious pressure, lifestyle changes, psychological trauma, child abuse etc.) and/or relationship disorders (performance anxiety, sexual incompatibility, loss of attraction, fears of intimacy etc. (Cole *et al.*, 1993).

ED is however more prevalent and severe among diabetics because most of the risk factors mentioned above overlap as comorbidities with diabetes. Vascular disease, hypertension, peripheral neuropathy and obesity are all more common in people with diabetes than in the general population. Diabetic neuropathies have been linked to ED in about 80% of men with diabetes. Diabetic neuropathies prevent correct neural transmission, so although the patient may be aroused, impulses are not relayed to the penis, causing reduced NO delivery to the smooth muscle of the corpus cavernosum. Diabetes can also cause damage to small arteries and arterioles. This impairs endothelium-dependent relaxation of penile smooth muscle preventing optimal blood flow to and from the penis, and maintenance of

an erection. In type 1 and type 2 diabetes, there is reduced production and increased consumption of NO due to reduction in eNOS. Additionally, poor glycaemic control can damage the walls of blood vessels of the penis and impair the NO signaling systems of the corpora cavernosa. Good control of glycaemia and blood pressure in men with diabetes is important to decrease the risk of microvascular and macrovascular complications and ED (Hood and Robertson, 2004).

Erectile dysfunction (ED) arises as a result of a collision of circumstances among any of a number of factors (e.g., risk factors, causes, probable associations), each with its own primary power to affect the outcome. Furthermore, each of the components has its own timing as part of a complex effort of compensation and adjustment that often obscures the individual details. In the end, ED results from a failure of local tissues or systemic supply and control structures. The power of any individual "cause" to degrade erectile function is an important but as-yet unquantified property. The power of a small abnormality over a long or critical period (e.g., organogenesis), or many small contributions, or multiple risk factors will certainly be greater than the sum of the individual elements. Without a full quantitation of pathways and their potential influence, one can compare the importance of causative factors only in limited ways. Not surprisingly, it is the presence of a multiplicity of unidentified or poorly understood causative factors that accounts in large measure for the current inability to cure and prevent ED.

There are two other important properties of a putatively causative factor for ED— reversibility and preventability— and these are strongly influenced by the time of onset and the duration of impact. Thus, a critical understanding that comes from recognizing the importance of the temporal associations of component factors is that the causes of ED in an individual may be guessed at but cannot be fully

disclosed by an analysis of a "snapshot" of the disease taken at the time of diagnosis (Heaton and Adams, 2004).

## 2.7 OTHER DETERMINANTS OF MALE SEXUAL DYSFUNCTION

### *2.7.1 Age*

Sexual dysfunction is an inevitable process of aging and thus prevalent in over 50% of men between 50 and 70 years of age (Rendell *et al.*, 1999). As men age the absolute number of leydig cells decrease by about 40% and the vigour of pulsating LH release is dampened. Free testosterone also decline by approximately 1.2% per year. These have contributed in no small measure tp prevalence of SD in the aged (Guay *et al.*, 2003b). Identification of the natural biologic changes that mediate sexual function in the aged is confounded by the effect of chronic illnesses and drugs in this age group. Changes in receptor site sensitivity may contribute to the age related decrease in sexual function (Schiavi *et al.*, 1990).

### *2.7.2 Smoking*

Cigarette smoking has been implicated to cause SD in both human and animal models and has been known to be associated with impaired arterial flow to the penis or acute vasospasm of the penile arteries. In one research the relative risk of developing arhterosclerosis in the penis and subsequent ED was 1.31 for each 10pack-years smoked (Mannino *et al.*, 1994).

### *2.7.3 Alcohol*

In small amounts alcohol is known to improve erection and increase libido as a result of its vasodilatory effect and the suppression of anxiety, however excessive consumption of alcohol or other recreational drugs may cause central sedation, reduced libido and transient erectile dysfunction either by a direct effect on the penile vascular system or by causing increased prolactin or reduced testosterone production (Stuart Hood and Mike Kirby, 2004)

### *2.7.4 Drugs*

Some pharmacological drugs particularly those in psychiatry have been associated with an effect on sexuality, even prescriptive medications such as antihypertensives and antidepressants have been shown to have an effect on sexual functioning. In men this effect includes decreased sex drive, erectile failure, decreased volume of ejaculate and delayed ejaculation.

### *2.7.5 Intravaginal ejaculatory latency time (IELT)*

An evidence based definition of premature ejaculation is important for the diagnosis and treatment of men complaining of premature ejaculation (Waldinger and Schweitzer, 2008). The Diagnostic and Statistical Manual, Fourth Edition, Text Revision (DSM-IV-TR) definition has been criticized for its vagueness and absence of a short ejaculation time criterion cut-off score (Waldinger and Schweitzer, 2006a). However, in 2008 and by consensus, the International Society for Sexual Medicine (ISSM) formulated the first evidence-based definition of lifelong premature ejaculation in which it has been defined as men with lifelong ejaculation within about 1 minute after vaginal penetration (McMahon *et al.*, 2008).

Recently, Waldinger proposed the existence of two other PE subtypes, e.g. Natural Variable PE and Premature-like Ejaculatory Dysfunction (Waldinger, 2006; Waldinger and Schweitzer, 2006b). Men with Premature-like Ejaculatory Dysfunction complain of PE while having normal ejaculatory times. In his classification of 4 PE subtypes, Waldinger emphasized that the 4 PE subtypes are characterized by different aetiologies and pathophysiologies (Waldinger, 2008). In two stopwatch measured surveys in the general male population of 5 Western countries, the median intravaginal ejaculation latency time (IELT) appeared 5.4 and 6.0 minutes, respectively (Waldinger *et al.*, 2005; Waldinger *et al.*, 2009). In these surveys, the prevalence of IELTs of less than 1 minute was about 2.5 %. In contrast, 28% of the investigated men considered to have a too short IELT. The

mean IELT of these men was 4.9 minutes. Besides these data, a study among sex therapists in Canada and the US showed that these sex therapists considered that a normal intercourse should last 3 to 7 minutes (Corty and Guardiani, 2008). The impact of the population involved, cultural differences, socio-economic level and the quality of psychosexual relationships on the perception of IELT could be significant.

### *2.7.6 Income levels*

People in higher income brackets have been shown to be more predisposed to developing obesity. Almost all countries (high-income and low-income alike) are experiencing an obesity epidemic, although with great variation between and within countries. In low-income countries, obesity is more common in middle aged women, people of higher socioeconomic status and those living in urban communities. In more affluent countries, obesity is not only common in the middle-aged, but is becoming increasingly prevalent among younger adults and children. Obesity has become a worldwide public health problem of epidemic proportions, as it may decrease life expectancy by 7 years at the age of 40 years. Excess bodyweight is now the sixth most important risk factor contributing to the overall burden of disease worldwide. Overweight and obesity may increase the risk of erectile dysfunction (ED) by 30–90% as compared with normal weight subjects. On the other hand, subjects with ED tend to be heavier and with a greater waist than subjects without ED (Esposito *et al.*, 2008).



## 2.8 METABOLIC SYNDROME

### *2.8.1 Dyslipidaemia*

Although clustering of some metabolic abnormalities was recognized as early as 1923, the coining of the term "syndrome X" in 1988 by Reaven renewed the impetus to conduct research concerning this syndrome. Unfortunately, the

definition of the metabolic syndrome is not as precise as the name implies. It is an umbrella term for a cluster of cardiovascular risk factors including increased central abdominal obesity, elevated triglycerides, reduced high-density lipoprotein, high blood pressure, increased fasting glucose, and hyperinsulinemia. These factors increase the risk of cardiovascular disease (CVD) and/or type 2 diabetes. Although the etiology of this syndrome is thought to stem from obesity and physical inactivity, the extent of interactions of the individual MetS components with one another remains poorly defined. Obesity, diabetes, hypogonadism, and specific hormone and metabolic profiles have been implicated in the pathophysiology of CVD (Traish *et al.*, 2009).



The use of the term "metabolic syndrome" has been debated and MetS has lacked an internationally accepted, uniform definition until recently (Pirkola *et al.*, 2008). In 1998, the World Health Organization (WHO) was the first organization to provide a definition of the metabolic syndrome. In response, the European Group for the Study of Insulin Resistance countered with a modification of the WHO definition. In 2001, the National Cholesterol Education Program (NCEP) released its definition. Subsequently, the American Association of Clinical Endocrinologists offered its views regarding the definition of the metabolic syndrome. The proliferation of definitions suggested that a single unifying definition was desirable. In the hope of accomplishing this, the International Diabetes Federation (IDF) proposed a new definition of the metabolic syndrome which emphasizes cntral adiposity as determined by ethnic group specific threshold of waist circumference (Ford, 2005).

Men with MetS have a higher risk for ED (Esposito and Giugliano, 2005). Because MetS increases CV risk, it is not surprising that ED may also be a predictor of subsequent CVD. Thompson *et al.*, (2003) studied over 9000 men in the Prostate Cancer Prevention Trial and the hazard ratio of men with new ED for CV events

over 5 years was 1.45. This is consistent with evidence presented by Corona *et al.*, (2006) in that 96.5% of their subjects with MetS exhibited ED, and Bansal *et al.*, (2005), who reported that in 154 men with organic ED, 43% had MetS and the percentage of individuals expressing MetS increased with increasing ED severity (Traish *et al.*, 2009).

MetS however does not manifest uniformly in all populations. Available evidences have shown that this syndrome is highly variable with ethnicity, lifestyle, age, and sex. Ford *et al.*, (2002) observed that a patient's age, sex and ethnicity invariably affects the development of the MetS. Guay et al., (2003a) showed that cigarette smoking, carbohydrate rich diets and physical inactivity all increases risk of developing the MetS. The prevalence of the MetS is very dependent on the definition used and one definition may not be applicable to a population of a different geographic area (Traish *et al.*, 2009). This was demonstrated by Lee *et al.*,*(2004)*. When they measured the prevalence of the MetS in 26,528 men in North Korea; they observed that NCEP ATP III definition underestimated the true prevalence as this population were naturally leaner in physique and thus suggested a lower threshold for central obesity should be used for such a population. This observation has been confirmed by Oh *et al.*, (2004).

### *2.8.2 Obesity*

Adipocytes are the main cellular constituents of adipose tissue and play an important role in regulating triglycerides and free fatty acids levels. Estrogen is a positive regulator of adipogenesis whilst androgens negatively regulates adipocyte differentiation, high levels of androgens both drive differentiation of the stem cells towards myogenesis thereby inhibiting adipogenesis. Aromatization of androgens to estrogen is associated with adipose tissue (McTernan *et al.*, 2002).

The metabolic syndrome is associated with a dysregulated adipose tissue; in part a consequence of adipose cell enlargement and the associated infiltration of

macrophages. Adipose cell enlargement leads to a proinflammatory state in the cells with reduced secretion of adiponectin and with increased secretion of several cytokines and chemokines including interleukin (IL)-6, IL-8, and MCP-1. MCP-1 has been shown to play an important role for the associated recruitment of macrophages into the adipose tissue. The increased release of cytokines leads to an impaired differentiation of the preadipocytes with reduced lipid accumulation and induction of adiponectin, thus promoting ectopic lipid storage. In particular tumor necrosis factor (TNF), but also IL-6, has been shown to induce these effects in preadipocytes and this is associated with an increased Wnt signaling maintaining the cells in an undifferentiated and proinflammatory state. The proinflammatory state in the adipose tissue also leads to a local insulin resistance including an impaired inhibitory effect of insulin on FFA release. The insulin resistance further supports the proinflammatory state because insulin, by itself, is both antilipolytic and anti inflammatory by antagonizing cytokine-induced activation of STAT signaling (Gustafson *et al.*, 2007).

A plausible biological mechanism for obesity induced hypogonadism may result in part from increased feedback inhibition of the hypothalamic-pituitary axis due to high levels of estrogen in obese men (Strain *et al.*, 1982). The subsequent reduction in circulating testosterone leads to increased deposits of visceral/abdominal adipose tissue (Marin, 1995).

## 2.9 ANDROGEN DEFICIENCY

Hypogonadism may be caused by genetic diseases such as klinefelters syndrome or 5 $\alpha$-reductase deficiency, congenital abnormalities including cryptorchidism or testicular feminization or testicular insults, such as trauma, mumps, orchitis, radiation or chemotherapy (Adamson and Baker, 2003). Hypogonadism in obese

men is characterized by high leptin levels. Leptin provides a physiological link between energy expenditure and reproduction and stimulates production of GnRH, In obese men leptin is unable to cross the blood brain barrier due to saturation and results in impaired stimulation of the release of GnRH thereby resulting in hypogonadism (Phillips *et al.*, 2010). While geography, ethnicity, lifestyle, age and gender all affect the development of MetS, low testosterone and sex hormone binding globulin, (SHBG) levels are considered risk factors for MetS, diabetes and cardiovascular disease. Selvin *et al.*, (2007) in their study from the Third National Health and Nutrition Examination Survey (NHANES III) reported that Low free and bioavailable testosterone concentrations in the normal range were associated with diabetes, independent of adiposity. They suggested that low androgen levels may be a risk factor for diabetes in men. In a multivariable model adjusted for age, ethnicity and adiposity they observed that men in the first tertile (lowest) of free testosterone level were four times more likely to have prevalent diabetes compared with men in the third tertile. Similarly, men in the first tertile of bioavailable testosterone also were approximately four times as likely to have prevalent diabetes compared with men in the third tertile, these associations persisted even after excluding men with clinically abnormal testosterone concentrations. They however observed no clear association for total testosterone after multivariable adjustment.



Chen *et al., (2002)* in their investigation of androgen deprivation therapy (ADT) on total body fat mass after 1-5yrs of treatment in 62 men with prostate cancer observed a significant increase in total body fat mass and a reduction in lean body mass.

Braga-Basaria *et al., (2006)* investigated men either treated with ADT or untreated and found a higher prevalence of MetS in men treated with ADT as compared to men untreated with ADT and the control group. BMI, triglycerides and FBS levels

were all significantly elevated in this study. In a double blind placebo controlled study of 13 men given 100 mg testosterone enanthate per week over 18 months. Katznelson *et al.,(1996)* observed a significant increase in fat free mass and a significant decrease in body fat mass. The role of androgens in the development of body fat mass is quite significant from these studies. It has been demonstrated that this relationship is even dose dependent. Wang *et al.,(2002)* demonstrated that the effect of 5mg testosterone patch on body fat reduction was less in comparism to a 100mg testosterone patch administered over the course of three months. However it has been suggested from evidence in various studies that testosterone administration is beneficial to only true hypogonadal men (Traish *et al.,* 2009).



# *Chapter 3*

# MATERIALS AND METHODS

## 3.1 PARTICIPANTS

A cross-sectional study was conducted among 300 diabetic patients visiting Tema General Hospital in the Greater Accra region of Ghana. The Participants were recruited in a consecutive procedure from November 2010 to March 2011. Eligibility criteria for participants were as follows: sexually active, stable heterosexual relation for at least 2 years before enrollment in the study, aged 18 years or older and diabetic. A stable relationship was defined as one in which the man was engaged and maintains sexual relations, regardless of their marital status. The age range of the diabetic men involved in this study was between 18 and 82 years. Participation of the respondents was voluntary and informed consent was obtained from each participant. The study was approved by the Committee on Human Research, Publication and Ethics of the School of Medical Science and the Komfo Anokye Teaching Hospital, Kumasi.



## 3.2 PROCEDURE

All participants were evaluated by using a semi-structured questionnaire and the Golombok Rust Inventory of Sexual Satisfaction (GRISS) which was translated into various local dialects for participants.

## 3.3 SOCIO-DEMOGRAPHIC AND ANTHROPOMETRIC DATA

A detailed self-designed semi-structured questionnaire was administered in a prefered local dialect to each consented study participant for socio-demographic information including age, marital status, behavioral activities (smoking and alcohol consumption), educational background, occupation and income level. Body weight with study participants in light clothing was measured to the nearest 0.1 kg on a bathroom scale (Zhongshan Camry Electronics Co. Ltd. Guangdong, China) and height to the nearest 0.5 cm was measured with the study participants standing upright and barefooted, with the heels put together and the head in the horizontal plane against a wall-mounted ruler. Body mass index (BMI) was calculated by dividing weight (kg) by the height squared ($m^2$). Waist circumference (to the nearest centimeter) was measured with a Gulick II spring-loaded measuring tape (Gay Mill, WI) midway between the inferior angle of the ribs and the suprailiac crest. Hip circumference was measured as the maximal circumference over the buttocks in centimeter and the waist to hip ratio (WHR) calculated by dividing the waist circumference (cm) by the hip circumference (cm).



## 3.4 MEASUREMENTS OF PERCEPTION OF IELT

Questions regarding perception of normal and abnormal IELT were adapted and modified from a study among sex therapists conducted in the US and Canada (Corty and Guardiani, 2008). The respondents were asked for background information (age, sex, occupation, educational level, marital status, etc.) and had questions about IELTs such as "too short," "adequate," "desirable," or "too long." The respondents were asked to give their opinion regarding, for example, "What is an *adequate* amount of time to elapse in sex from penile penetration of the vagina to ejaculation?" The question was asked in four different ways, with the italicized

word changing from *adequate,* to *desirable,* to *too short,* to *too long*. This is an estimated time response, not a stop-watch-measured time response.

## 3.5 THE GOLOMBOK RUST INVENTORY OF SEXUAL SATISFACTION

Sexual response was measured by the Golombok Rust Inventory of Sexual Satisfaction (GRISS) questionnaire. The GRISS has 28 items on a single sheet and its use for assessing the existence and severity of sexual problems in heterosexual couples or individuals who have a current heterosexual relationship. All the 28 questions were answered on a five-point (Likert type) scale from "always", through "usually', "sometimes", and "hardly ever", to "never". It provided overall scores of the quality of sexual functioning within a relationship. In addition, subscale scores of impotence, premature ejaculation, infrequency, non-communication, dissatisfaction, non-sensuality and avoidance were obtained and represented as a profile. Responses were summed up to give a total raw score (range 28-140). The total score and subscale scores were transformed using a standard nine point scale, with high scores indicating greater problems. Scores of five or more were considered to indicate SD. The GRISS was chosen because it is standardized, easy to administer and score, relatively unobtrusive and substantially inexpensive.

The GRISS can be used to assess improvement as a result of sexual or marital therapy and to compare the efficacy of different treatment methods. It can also be used to investigate the relationship between sexual dysfunction and extraneous variables. The subscales are particularly helpful in providing a profile for diagnosis of the pattern of sexual functioning within the couple, which can be of great benefit in designing a treatment program. The reliability of the overall scales has been found to be 0.94 for men and that of the subscales on average 0.74 (ranging

between 0.61 and 0.83). Validity has been demonstrated under a variety of circumstances (Rust and Golombok, 1985; Rust and Golombok, 1986b; Rust and Golombok, 1986a).

## 3.6 SAMPLE COLLECTION, PREPARATION AND ANALYSIS

Six milliliters (6 ml) of venous blood sample was collected from each participant in the morning between 07.00 to 09.00 GMT into Ethylenediaminetetraacetic acid (EDTA) vacutainer® tubes, Fluoride oxalate tube and evacuated gel tubes for serum preparation (Becton Dickinson, Rutherford, NJ). Samples in the EDTA tubes and fluoride oxalate tubes were used for HbA1c and fasting blood glucose measurement using BT 5000® Random Access Chemistry Analyzer (Biotecnica, Italy) while samples in the evacuated gel tubes were centrifuged at 3000 g for 5 minutes and the serum aliquoted and stored in cryovials at a temperature of -80oC until time for testosterone assay using the AxSYM automated analyzer (Abbott Diagnostics, USA) and lipid profile which include total cholesterol (T-CHO), triglycerides (TAG), high density lipoprotein (D-HDL) and low density lipoprotein (LDL) were determined using BT 5000® Random Access Chemistry Analyzer (Biotecnica, Italy), the Vital Diagnostic kits were used. The AxSYM uses Micro-particle Enzyme Immunoassay in the determination of Testosterone. The methods adopted by the automated instruments for the determination of biochemical parameters were done according to the reagent manufacturers' instructions (JAS Diagnostics, Inc. Miami Florida, USA and Abbott Diagnostics, USA).

## 3.7 BIOCHEMICAL ASSAYS

### *3.7.1 Glucose*

Glucose level was measured using the hexokinase method which is linked to the production of NADH. The enzyme hexokinase phosphorylates glucose with ATP to produce glucose-6 –phosphate

***Glucose + ATP → Glucose-6-phosphate +ADP***

Glucose-6-phosphate dehydrogenase enzyme then oxidized Glucose-6-phosphate to 6-phosphogluconate with a reduction of NAD to NADH

***Glucose-6-phosphate + NAD → 6-Phosphogluconate + NADH***

The amount of NADH produced in this reaction is directly proportional to the amount of glucose in the original sample. By measuring the absorbance of NADH at 340 nm the amount of glucose in the sample can be determined.

### *3.7.2 Cholesterol*

**Principle and Method:** The present method utilized a phenol substitute (4-aminoantipyrine (4-AAP)) that performed like phenol but without being corrosive. The intensity of the red colour produced was directly proportional to the total cholesterol in the sample when read at 500 nm.

$$\textbf{Cholesterol Esters} \xrightarrow{\textbf{Cholesterol Esterase}} \textbf{Cholesterol} + \textbf{Fatty Acids}$$

$$\textbf{Cholesterol} + O_2 \xrightarrow{\textbf{Cholesterol oxidase}} \textbf{Cholest} - 4 - en - 3 - one + H_2O$$

$$2H_2O_2 + HBA + 4AAP \xrightarrow{\textbf{Peroxidase}} \textbf{Quinoneimine (red dye)} + 4H_2O$$

### *3.7.3 Triglycerides*

**Principle and Method:** A modified Trinder method was used. (Trinder, 1969; Barham and Trinder, 1972) colour reaction to produce a fast, linear, endpoint reaction (Fossati and Prencipe, 1982; McGowan *et al.*, 1983). Triglycerides in the

sample are hydrolyzed by lipase to glycerol and fatty acids. The glycerol is then phosphorylated by ATP to glycerol-3-phosphate (G3P) and ADP in a reaction catalyzed by glycerol kinase. G3P is then converted to dihydroxyacetone phosphate (DAP) and hydrogen peroxide by glycerophosphate oxidase (GPO). The hydrogen peroxide then reacts with 4-aminoantipyrine (4-AAP) and 3, 5-dichloro-2-hydroxybenzen (3,5-DHBS) in a reaction catalyzed by peroxidase to yield a red coloured quinoneimine dye. The intensity of the colour produced is directly proportional to the concentration of triglycerides in the sample.



$$\textbf{Triglycerides} + H_2O \xrightarrow{\textit{Lipase}} \textit{Glycerol} + \textit{Fatty Acids}$$

$$\textbf{Glycerol} + ATP \xrightarrow{\textit{Glycerol kinase}} G3P + ADP$$

$$\textbf{G3P} + O_2 \xrightarrow{\textit{Glycerolphosphate oxidase}} DAP + H_2O_2$$

$$H_2O_2 + 4AAP + 3,5-DHBS \xrightarrow{\textit{Peroxidase}} \textit{Quinoneimine (red dye)} + 2H_2O$$

### *3.7.4 HDL-Cholesterol*

**Principle and Method:** The method employed herein is in a two reagent format. The first reagent contains anti human β-lipoprotein antibody which binds to lipoproteins (LDL, VLDL and chylomicrons) other than HDL. The second reagent contains enzymes which then selectively react with the cholesterol present in the HDL particles. Consequently only HDL cholesterol is subject to cholesterol measurement. The primary reading is done at 600 nm and secondary at 700 nm.

### *3.7.5 LDL- cholesterol*

LDL-Cholesterol was calculated from TOT- Cholesterol, HDL-Cholesterol and Triglycerides in a formula as follows

***LDL-Cholesterol = Total Cholesterol - HDL-cholesterol (0.16 x Triglycerides)***

### 3.7.6 *Glycated haemoglobin*

The method utilizes the interaction of antigen and antibody to directly determine the HbA1c in whole blood. Total hemoglobin and HbA1c have the same unspecific absorption rate to latex particles, when a mouse antihuman HbA1c monoclonal antibody is added (R2), latex- HbA1c-mouse antihuman HbA1c antibody complex is formed. Agglutination is formed when goat antimouse igG polyclonal antibody interacts with the monoclonal antibody. The amount of agglutination is proportional to the amount of HbA1c absorbed on to the surface of latex particles. The amount of agglutination is measured as absorbance at 660nm. The HbA1c value is obtained from a calibration curve.



### 3.7.7 *Testosterone*

The AxSYM testosterone measurement utilizes a displacement method by displacing testosterone from its normally bound protein which is sex hormone binding globulin (SHBG) or testosterone binding globulin (TeBG) and albumin. Testosterone is displaced from these proteins and thus measured. This technique is based on a Microparticle Enzyme Immunoassay (MEIA). In the first phase sample, Anti-testosterone coated microparticle is pipetted into a well. Testosterone alkaline phosphatase conjugate is then added. Wash buffer is then added. Testosterone in the mixture binds to the antitestosterone microparticle to form an antibody-antigen complex. Washing is then done to remove conjugate not bound to the microparticle. The substrate 4-methylumbelliferyl phosphate (MUP) is added to the matrix cell, the alkaline phosphatase labeled conjugate catalyzes the removal of a phosphate group from the substrate yielding a fluorescent product called 4-methylumbelliferone. The fluorescent product is measured by the MEIA optical assembly. The rate of signal development is inversely proportional to the amount of testosterone in the specimen. Testosterone concentrations are calculated using a stored calibration curve which is ordinarily stable for at least two weeks.

## 3.8 METABOLIC SYNDROME DEFINITIONS

### *3.8.1 National Cholesterol Education Program, Adult Panel III (NCEP ATP III) criteria*

Metabolic syndrome as defined according to the criteria of the National Cholesterol Education Program, Adult Treatment Panel III (NCEP ATP III) to include individuals with any three or more of the following five components: (1) abdominal obesity-ATP III (waist circumference > 102 cm); (2) high TG ≥ 1.7 mmol/L (150 mg/dl); (3) low HDL-C : < 0.9 mmol/L (< 40 mg/dl); and (4) High BP (systolic BP ≥ 130 mm Hg or diastolic BP ≥ 85 mm Hg or treatment of hypertension); and (5) high fasting glucose ≥ 6.1 mmol/l (NCEP, 2001).



### *3.8.2 International Diabetes Federation (IDF) criteria*

According to the new definition by the International Diabetes Federation (IDF) (Alberti et al., 2006), metabolic syndrome was diagnosed if central obesity (waist measurement >90 cm) is accompanied by any 2 of the following 4 factors: (1) TG levels of 1.7 mmol/L or greater, (2) an HDL cholesterol lower than 1.03 mmol/L, (3) a blood pressure (BP) of 130/85 mm Hg or greater or treatment of previously diagnosed hypertension, and (4) a fasting blood glucose (FBG) of 5.6 mmol/L or greater or previously diagnosed type 2 diabetes.

### *3.8.3 World Health Organization (WHO) criteria*

World Health Organization criteria (Alberti et al., 2005) required presence of diabetes mellitus, impaired glucose tolerance or insulin resistance and any two of the following: (1) Body mass index (BMI) ≥30 kg/m2 and/or waist-to-hip ratio >0.90, (2) blood pressure ≥140/≥90 mmHg or on medication, (3) diabetes ≥6.1 mmol/L or on medication for diabetes, impaired glucose tolerance or insulin resistance, (4) triglyceride ≥1.7 mmol/L and/or HDL-C <0.91 mmol/L.

## 3.9 STATISTICAL ANALYSIS

Continuous data were presented as mean ± SD whilst categorical data presented as percentages. Continuous data were compared using unpaired *t*-test and categorical data compared using Chi-square analysis. Logistic regression was used to assess the simultaneous influence of different variables in sexuality. In all statistical tests, a value of $p<0.05$ was considered significant. The entry of the variables into the model was considered if p value is less than 0.05, and a stepwise procedure was applied. All analysis were performed using Sigma Plot for Windows, Version 11.0, (Systat Software, Inc. Germany) .



# *Chapter 4*

# RESULTS

## 4.1 RESPONSE RATE AND SOCIO-DEMOGRAPHIC CHARACTERISTIC

Out the 300 subjects interviewed, 20 refused to be part of this study leaving 280 respondents. Six (6) of the respondents had incomplete data leaving 274 evaluable data, giving a response rate of 91.3%. All the respondents had at least basic education with 39.1%, 15.7% and 10.6% having secondary, technical and tertiary education respectively. 97.4% of respondents were married, 65.3% were hypertensive, 3.3% smoked cigarettes, 27% took alcoholic beverages and 32.8% did some form of exercise.

## 4.2 INFLUENCE OF METABOLIC SYNDROME ON SD AMONG DIABETIC PATIENTS

### *4.2.1 General features*

The mean age as well as the mean duration of diabetes from this study was 59.9 ± 11.3 and 6.8 ± 5.9 years respectively. The mean blood pressure, BMI and WHR of the studied population were 151.5 ± 24.7/96.2 ± 17.7 mmHg, 26.3 ± 4.1 kg $m^{-2}$ and 0.9 ± 0.2 respectively. However, when the studied population was stratified based on sexual function, those with sexual dysfunction were significantly older, have been with diabetes for a longer period, were heavier has measured by weight and BMI as well as having higher mean systolic and diastolic blood pressure (Table 4.1).

*Result*

There was no significant difference in the mean FBG and lipid profile when the studied participants were classified based on sexual function. However, pulling together, the mean FBG, total cholesterol and HDL-cholesterol of the studied participant were 9.4 ± 4.0 mmol $L^{-1}$, 5.2 ± 1.2 mmol $L^{-1}$ and 1.2 ± 0.3 mmol $L^{-1}$ respectively (Table 4.1). The mean score when metabolic syndrome was diagnosed using WHO, NCEP ATP III and IDF criteria were 3.2 ± 0.9, 2.4 ± 1.0 and 2.9 ± 1.0 respectively despite the fact that there were no significant difference when the population was stratified based on sexual function (Table 4.1).

The raw score for sexual dysfunction and its sub-scales were significantly higher among those with sexual dysfunction as compared to those without sexual dysfunction as shown in Table 4.1.

**Table 4.1 General characteristic of the study population stratified by sexual dysfunction.**

| Variables | Total (n=274) | NSD (n=84) | SD (n=190) | P value |
|---|---|---|---|---|
| *Socio-demographic data* | | | | |
| Age (years) | 59.9 ± 11.3 | 56.2 ± 11.6 | 65.1 ± 7.5 | < 0.0001 |
| Duration of diabetes (yrs) | 6.8 ± 5.9 | 6.0 ± 5.6 | 8.5 ± 6.2 | 0.0012 |
| ***Anthropometric data*** | | | | |
| SBP (mmHg) | 151.5 ± 24.7 | 148.8 ± 25.7 | 157.6 ± 21.1 | 0.0063 |
| DBP (mmHg) | 96.2 ± 17.7 | 94.8 ± 16.9 | 99.4 ± 19.1 | 0.0504 |
| Weight (kg) | 76.0 ± 14.3 | 72.6 ± 10.3 | 77.6 ± 15.5 | 0.0078 |
| BMI (kg $m^{-2}$) | 26.3 ± 4.1 | 25.5 ± 3.0 | 26.6 ± 4.5 | 0.0557 |
| Hip circumference (cm) | 100.7 ± 9.5 | 100.0 ± 7.6 | 101.0 ± 10.3 | 0.4559 |
| Waist circumference (cm) | 94.5 ± 16.0 | 94.6 ± 16.3 | 94.4 ± 15.9 | 0.9025 |
| WHR | 0.9 ± 0.2 | 0.9 ± 0.2 | 0.9 ± 0.1 | 0.5362 |
| ***Biochemical parameters*** | | | | |
| FBG (mmol $L^{-1}$) | 9.4 ± 4.0 | 9.3 ± 3.4 | 9.4 ± 4.2 | 0.8254 |
| Total cholesterol (mmol $L^{-1}$) | 5.2 ± 1.2 | 5.1 ± 1.1 | 5.3 ± 1.3 | 0.2021 |
| Triglyceride (mmol $L^{-1}$) | 1.4 ± 0.7 | 1.4 ± 0.8 | 1.5 ± 0.7 | 0.3137 |
| HDL-cholesterol (mmol $L^{-1}$) | 1.2 ± 0.3 | 1.2 ± 0.3 | 1.2 ± 0.3 | 0.5161 |
| LDL-cholesterol (mmol $L^{-1}$) | 3.3 ± 1.1 | 3.3 ± 1.0 | 3.5 ± 1.2 | 0.1279 |
| ***Metabolic syndrome scores*** | | | | |
| WHO | 3.2 ± 0.9 | 3.1 ± 1.0 | 3.2 ± 0.9 | 0.4658 |
| NCEP ATP III | 2.4 ± 1.0 | 2.3 ± 1.0 | 2.5 ± 1.0 | 0.2534 |
| IDF | 2.9 ± 1.0 | 2.8 ± 1.0 | 3.0 ± 1.0 | 0.0993 |
| ***Raw score for sexual dysfunction and its sub-scales*** | | | | |
| Sexual dysfunction | 72.2 ± 10.6 | 58.8± 8.0 | 78.1 ± 4.4 | < 0.0001 |
| Impotence | 11.3 ± 2.1 | 9.2 ± 1.6 | 12.3 ± 1.6 | < 0.0001 |
| Premature ejaculation | 7.4 ± 2.9 | 4.8 ± 1.5 | 8.5 ± 2.6 | < 0.0001 |
| Non-sensuality | 11.6 ± 2.5 | 9.2 ± 2.2 | 12.7 ± 1.7 | < 0.0001 |
| Avoidance | 8.0 ± 3.2 | 7.8 ± 4.5 | 8.1 ± 2.5 | 0.5710 |
| Dissatisfaction | 11.3 ± 1.6 | 10.0 ± 1.7 | 11.8 ± 1.2 | < 0.0001 |
| Non-communication | 4.2 ± 1.5 | 3.0 ± 1.1 | 4.8 ± 1.3 | < 0.0001 |
| Infrequency | 5.3 ± 1.4 | 5.1 ± 1.4 | 5.4 ± 1.4 | 0.0796 |

### 4.2.2 *Prevalence of Metabolic Syndrome*

The prevalence of MetS as defined by the various criteria was 78.8%, 43.4% and 51.8% for WHO, NCEP ATP III and IDF respectively. Even though the prevalence of MetS was found to be higher among those with SD irrespective of the criteria used, the difference did not reach a significant level (Table 4.2). About 80%, 40% and 60% of the studied population had MetS score of 3 or more using WHO, NCEP ATP III and IDF criteria respectively. Classification according to sexual function indicates that those with SD generally have a lower rate of MetS score of 1 and 2 but higher rates of MetS score of 3 or more notwithstanding the fact that the difference did not reach a significant level (Table 4.2).



As shown in table 4.3, aside raised fasting blood glucose, the most predominant contributor to the prevalence of MetS was central obesity (76.6%) followed by raised blood pressure (59.5%) and dyslipidaemia (47.8%) using WHO criteria. The most predominant components are raised blood pressure (73.0%) followed by raised triglyceride (32.1%), reduced HDL-cholesterol (28.5%) and abdominal obesity (19.3%) using the NCEP ATP III criteria. According to IDF criteria, the most predominant components are raised blood pressure (73.0%) followed by abdominal obesity (65.0%), raised triglyceride (32.1%) and reduced HDL-cholesterol (28.5%) (Table 4.3). When the studied participant were grouped based on sexual function, those with SD have significantly ($p=0.0482$) higher rate of central obesity (80.0%) as compared to those without SD (69.0%) using WHO criteria. But when NCEP ATP III and IDF criteria were applied, raised blood pressure was more common among those with SD as compared to those without SD (Table 4.3).

**Table 4.2 Prevalence of metabolic syndrome and metabolic score among the studied population stratified by sexual function**

| Variable | Total (n=274) | NSD (n=84) | SD (n=190) | P value |
|---|---|---|---|---|
| *Prevalence of MetS* | | | | |
| WHO | 216(78.8%) | 64(76.2%) | 152(80.0%) | 0.4766 |
| NCEP ATP III | 119(43.4%) | 35(41.7%) | 84(44.2%) | 0.6953 |
| IDF | 142(51.8%) | 43(51.2%) | 99(52.1%) | 0.8889 |
| *Prevalence of clustering of components of MetS* | | | | |
| **WHO** | | | | |
| 0 | 0(0.0%) | 0(0.0%) | 0(0.0%) | |
| 1 | 11(4.0%) | 4(4.8%) | 7(3.7%) | 0.6752 |
| 2 | 46(16.8%) | 16(19.0%) | 30(15.8%) | 0.5059 |
| ≥3 | 217(79.2%) | 64(76.2%) | 153(80.5%) | 0.4149 |
| **NCEP ATP III** | | | | |
| 0 | 3(1.1%) | 0(0.0%) | 3(1.6%) | 0.2469 |
| 1 | 46(16.8%) | 13(15.5%) | 33(17.4%) | 0.6992 |
| 2 | 107(39.1%) | 34(40.5%) | 73(38.4%) | 0.7478 |
| ≥3 | 118(43.1%) | 32(38.1%) | 86(45.3%) | 0.2692 |
| **IDF** | | | | |
| 0 | 1(0.4%) | 0(0.0%) | 1(0.5%) | 0.5053 |
| 1 | 20(7.2%) | 8(9.5%) | 12(6.3%) | 0.3466 |
| 2 | 87(31.8%) | 31(36.9%) | 56(29.5%) | 0.2231 |
| ≥3 | 166(60.6%) | 49(58.3%) | 117(61.6%) | 0.6122 |

*Data are presented as a proportion with corresponding percentages in parenthesis.*
*The proportions were compared using Chi square test.*

**Table 4.3 Prevalence of the various metabolic syndrome risk factors among the study population Classified by sexual function**

| Variable | Total (n=274) | NSD (n=84) | SD (n=190) | P value |
|---|---|---|---|---|
| **WHO** | | | | |
| Central Obesity – WHR | 210(76.6%) | 58(69.0%) | 152(80.0%) | 0.0482 |
| Raised fasting glucose | 274(100.0%) | 84(100.0%) | 190(100.0%) | |
| Hyperlipidaemia | 131(47.8%) | 36(42.9%) | 95(50.0%) | 0.2751 |
| Raised blood pressure | 163(59.5%) | 47(56.0%) | 116(61.1%) | 0.4278 |
| **NCEP ATP III** | | | | |
| Abdominal Obesity – WC | 53(19.3%) | 13(15.5%) | 40(21.1%) | 0.2813 |
| Raised fasting glucose | 274(100.0%) | 84(100.0%) | 190(100.0%) | |
| Raised Triglyceride | 88(32.1%) | 25(29.8%) | 63(33.2%) | 0.5788 |
| Raised blood pressure | 200(73.0%) | 54(64.3%) | 146(76.8%) | 0.0309 |
| Reduced HDL-C | 78(28.5%) | 21(25.0%) | 57(30.0%) | 0.3978 |
| **IDF** | | | | |
| Abdominal Obesity – WC | 178(65.0%) | 52(61.9%) | 126(66.3%) | 0.4804 |
| Raised fasting glucose | 274(100.0%) | 84(100.0%) | 190(100.0%) | |
| Raised Triglyceride | 88(32.1%) | 25(29.8%) | 63(33.2%) | 0.5788 |
| Raised blood pressure | 200(73.0%) | 54(64.3%) | 146(76.8%) | 0.0309 |
| Reduced HDL-C | 78(28.5%) | 21(25.0%) | 57(30.0%) | 0.3978 |

***Data are presented as a proportion with corresponding percentages in parenthesis.***
***The proportions were compared using Chi square test***

### *4.2.3 Interplay between SD, MetS, anthropometric and biochemical assay*

From the partial correlational analysis, there is general positive association between indicators of sexual function and age, blood pressure as well as duration of diabetes except for infrequency (INF). Whereas impotence correlates positively with weight and BMI, avoidance correlate positively with FBG and TG but negatively with weight and non-communication is associated positively with WHR, total cholesterol and LDL-cholesterol. Also, infrequency correlates positively with TG as shown in Table 4.4. Except for impotence and non-communication, SD and its subscales correlate positively with MetS score irrespectively of the criteria used (Table 4.4).



**Table 4.4 Partial correlations between sexual dysfunction parameters and determinants of metabolic syndrome**

| Variable | SD | IMP | PE | NS | AV | DIS | NC | INF |
|---|---|---|---|---|---|---|---|---|
| Age | **0.39*** ** | **0.31*** ** | **0.33*** ** | **0.39*** ** | 0.15* | 0.24*** | 0.21*** | -0.06 |
| SBP | 0.23*** | 0.15* | 0.27*** | 0.23*** | 0.02 | 0.22*** | 0.08 | 0.05 |
| DBP | 0.19** | 0.15* | 0.21*** | 0.17** | -0.01 | 0.24*** | 0.06 | 0.09 |
| DOD | 0.26*** | 0.11 | 0.27*** | 0.20*** | 0.00 | 0.27*** | 0.09 | 0.05 |
| WT | 0.08 | 0.17** | 0.06 | -0.06 | -0.12* | 0.04 | 0.02 | -0.04 |
| BMI | 0.01 | 0.14* | 0.02 | -0.04 | -0.02 | -0.06 | -0.06 | 0.01 |
| WC | 0.04 | 0.11 | -0.04 | -0.10 | -0.03 | -0.09 | -0.08 | -0.05 |
| WHR | 0.01 | 0.08 | -0.05 | 0.03 | 0.10 | 0.03 | 0.13* | 0.02 |
| FBG | 0.06 | 0.05 | 0.04 | 0.04 | 0.16** | -0.07 | 0.00 | 0.09 |
| TC | 0.05 | 0.05 | -0.02 | -0.04 | 0.01 | -0.03 | 0.18** | -0.04 |
| TG | 0.14 | 0.04 | -0.09 | -0.02 | 0.23*** | -0.03 | 0.03 | 0.29*** |
| HDL-c | 0.05 | 0.11 | 0.03 | 0.06 | 0.00 | 0.03 | 0.03 | 0.02 |
| LDL-c | 0.06 | 0.00 | -0.02 | -0.09 | 0.10 | -0.04 | 0.18** | 0.01 |
| WHO | 0.16** | 0.08 | 0.17** | 0.16** | 0.10 | 0.15* | 0.00 | 0.15* |
| ATP | 0.16** | 0.01 | 0.13* | 0.12* | 0.14* | 0.11 | 0.08 | 0.19** |
| IDF | 0.21*** | 0.08 | 0.17** | 0.22*** | 0.14* | 0.16** | 0.06 | 0.16** |



***Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed), ***Correlation is significant at the 0.001 level (2-tailed). Boldface r = Pearson product moment correlation coefficient with a medium size ($0.30 \leq r \geq 0.50$) effect.**

## 4.3 DETERMINANTS OF SD AMONG DIABETIC PATIENTS

### *4.3.1 General feature*

The mean age, weight, BMI and income level of the study population was 59.9 ± 11.3 years, 76.0 ± 14.3kg, 26.8 ± 9.8 kg $m^{-2}$ and Ghc 212.9 ± 200.6 respectively from the socio-demographic characteristic in Table 4.5. When the study population was stratified based on SD, those with SD were significantly older ($p < 0.0001$), heavier ($p = 0.0078$ for weight and $p = 0.0462$ for BMI) and had higher income level ($p = 0.0033$) as compared to those without SD (Table 4.1). The mean testosterone level was significantly lower ($p = 0.0250$) when those with SD (6.0 ± 2.1 ng $mL^{-1}$) were compared to those without SD (6.7 ± 2.8 ng $mL^{-1}$). However, the mean stanine scores as derived from the various SD subscales were significantly higher among those with SD as compared to those without SD as shown in Table 4.5.

**Table 4.5 General characteristic of the study population stratified by sexual dysfunction**

| Variables | Total | NSD | SD | P value |
|---|---|---|---|---|
| *Socio-demographic data* | | | | |
| Age (yrs) | 59.9 ± 11.3 | 57.2 ± 11.6 | 66.1 ± 7.5 | < 0.0001 |
| Weight (kg) | 76.0 ± 14.3 | 72.6 ± 10.3 | 77.6 ± 15.5 | 0.0078 |
| Height (m) | 1.7 ± 8.2 | 1.7 ± 7.1 | 1.7 ± 8.6 | 0.1840 |
| BMI (kg $m^{-2}$) | 26.8 ± 9.8 | 25.5 ± 3.0 | 26.6 ± 4.5 | 0.0462 |
| Income level (Ghc) | 212.9 ± 200.6 | 159.7 ± 81.5 | 236.6 ± 231.4 | 0.0033 |
| *Perceived intra-vaginal ejaculatory latency time* | | | | |
| Adequate (min.) | 8.2 ± 4.7 | 7.4 ± 2.5 | 8.8 ± 5.3 | 0.0275 |
| Desirable (min.) | 8.5 ± 4.9 | 7.7 ± 2.6 | 9.1 ± 5.6 | 0.0259 |
| Too short (min.) | 1.6 ± 1.4 | 1.3 ± 0.7 | 1.7 ± 1.5 | 0.0101 |
| Too long (min.) | 24.2 ± 10.9 | 25.5 ± 8.1 | 23.7 ± 11.9 | 0.2046 |
| *Biochemical data* | | | | |
| FBG (mmol $L^{-1}$) | 9.4 ± 4.0 | 9.3 ± 3.4 | 9.4 ± 4.2 | 0.8317 |
| Testosterone (ng $mL^{-1}$) | 6.3 ± 2.5 | 6.7 ± 2.8 | 6.0 ± 2.1 | 0.0250 |
| HbA1c (%) | 8.6 ± 1.9 | 8.7 ± 2.1 | 8.6 ± 1.8 | 0.7354 |
| *Sexual dysfunction subscales* | | | | |
| Impotence | 5.2 ± 2.0 | 3.4 ± 1.6 | 6.2 ± 1.4 | < 0.0001 |
| Premature ejaculation | 4.9 ± 1.8 | 3.4 ± 0.9 | 5.6 ± 1.7 | < 0.0001 |
| Non-sensuality | 5.1 ± 1.9 | 3.3 ± 1.7 | 5.8 ± 1.3 | < 0.0001 |
| Avoidance | 4.9 ± 1.8 | 4.9 ± 2.4 | 4.9 ± 1.5 | 0.9507 |
| Dissatisfaction | 5.0 ± 1.8 | 3.5 ± 1.9 | 5.7 ± 1.4 | < 0.0001 |
| Non-communication | 5.0 ± 1.9 | 3.3 ± 1.6 | 5.7 ± 1.5 | < 0.0001 |
| Infrequency | 5.2 ± 1.8 | 4.9 ± 1.8 | 5.3 ± 1.8 | 0.0874 |

***Data are presented as mean ± Std. Dev. Participant without sexual dysfunction (NSD) were compared with those with sexual dysfunction (SD) using unpaired t-test.***

### 4.3.2 *Sexual function-GRISS*

The sexual function scores of the participants for each GRISS subscale are shown in Figure 4.1. All the respondents had one or more subscale scores reflecting sexual problems (score of 5 or above). The prevalence of SD among the respondents in this study is 69.3% (i.e. 190 out of 274). The most prevalent areas of difficulty were infrequency (217 of 274, 79.2%), non-sensuality (204 out of 274, 74.5%), dissatisfaction with sexual acts (197 of 274, 71.9%), non-communication (194 of 274, 70.8%), impotence (186 out of 274, 67.9%), premature ejaculation (155 out of 274, 56.6%) and avoidance (117 out of 274, 42.7%).



However, severe SD was seen in 4.7% of the studied population (i.e. 13 out 274). Also the most prevalent areas of severe difficulty were impotence with (39 of 274, 14.2%), avoidance (30 out of 274, 10.9%), premature ejaculation (24 out of 274, 8.8%), non-sensuality (20 out of 274, 7.3%), infrequency (11 out of 274, 4.0%), dissatisfaction (10 out of 274, 3.6%) and non-communication (9 out of 274, 3.3%) (Figure 4.1).

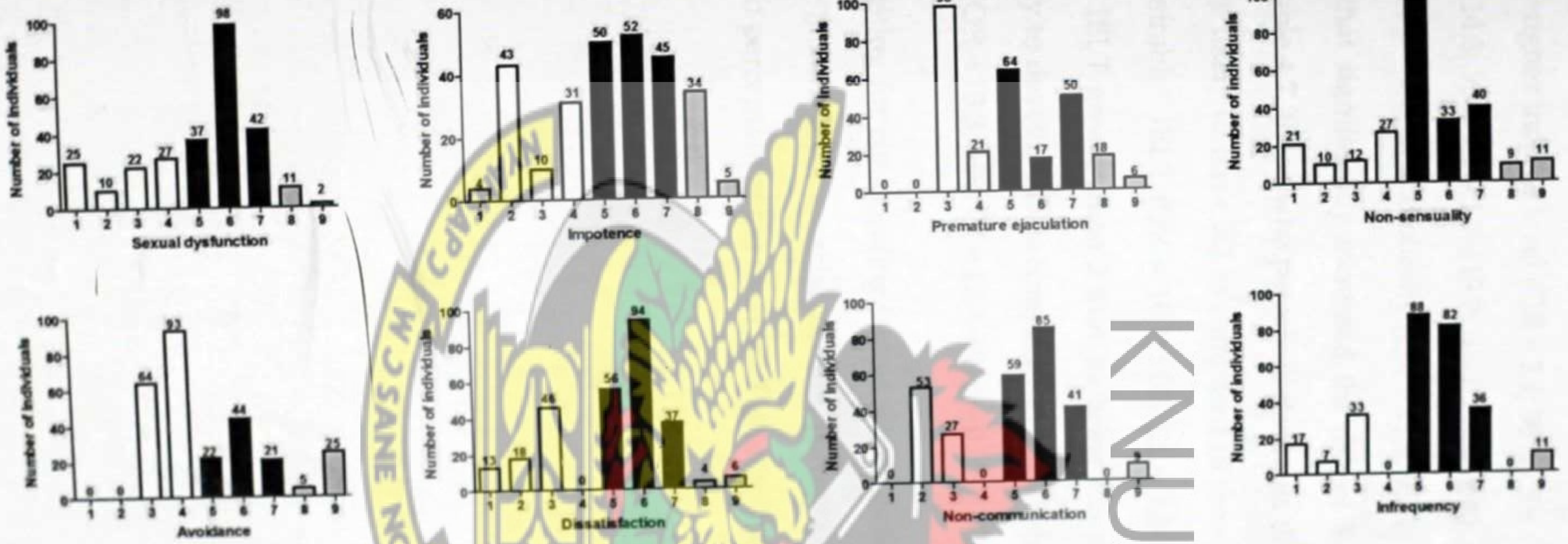


**Figure 4.1 Scores of sexual dysfunction in 274 studied population according to GRISS questionnaire.**

Graph shows the distribution of scores (from 1 to 9 on the x- axis) for each GRISS subscale, with the number of patients (y-axis) above each score. Normal scores are 1 to 4 (clear columns), abnormal scores are 5 to 9 (shaded columns) and severe abnormal scores are 8 and 9 (grey columns).

### *4.3.3 Risk factors*

The effect of different socio-demographic variables on the SD risk is recorded in Table 4.6. Higher income level (OR = 2.1; 95% CI = 1.0-4.3; p = 0.042 for Ghc 111-400 and OR = 14.3; 95% CI = 1.7-119.7; p = 0.014 for Ghc > 400), exercise (OR = 2.2; 95% CI = 1.3-3.7; p = 0.004) and obesity (OR = 11.9; 95% CI = 2.7-52.8; p = 0.001) were the variables that significantly increased the risk of SD from the univariate analysis. Also, in Table 4.7, those who perceived desirable IELT higher than 13 min. were 10 times more likely to have SD as compared to those who perceived 7 to 13 min. as being "desirable" IELT (OR = 10.1; 95% CI = 1.3-77.9; p = 0.026) and those who perceived IELT greater than 2 min. as being too short are also at about 13 times more likely to develop SD as compared to those who perceived 1 to 2 min. as being too short (OR = 13.3; 95% CI = 1.8-99.9; p = 0.012) (Table 4.7).

After adjusting for confounding factors which includes age, the risk factors for SD are higher income level, exercise, obesity, perception of desirable IELT greater than 13 min and perception of too short IELT greater than 2 min. (Table 4.6 and 4.7).

**Table 4.6 Rate of sexual dysfunction according to socio-demographic risk factors**

| Variables | n/N* | Rate of SD (%) | OR(95% CI | P value | aOR(95% CI | P value |
|---|---|---|---|---|---|---|
| *Marital status* | | | | | | |
| Married | 185/267 | 69.3 | 0.9(0.2-4.7) | 0.904 | 1.7(0.2-15.3) | 0.628 |
| Single | 5/7 | 71.4 | | | | |
| *Educational level* | | | | | | |
| Basic | 68/95 | 71.6 | | | | |
| Secondary | 71/107 | 66.4 | 0.78(0.43-1.4) | 0.424 | 0.5(0.3-1.1) | 0.087 |
| Technical | 27/43 | 62.8 | 0.67(0.31-1.45) | 0.303 | 0.6(0.3-1.5) | 0.283 |
| Tertiary | 24/29 | 82.8 | 1.91(0.7-5.5) | 0.234 | 1.5(0.5-5.1) | 0.464 |
| *Income level* | | | | | | |
| No income | 4/13 | 30.8 | 2.1(0.5-7.7) | 0.309 | 2.9(0.7-12.5) | 0.152 |
| <111 | 19/36 | 52.8 | | | | |
| 111-400 | 146/208 | 70.2 | 2.1(1.0-4.3) | 0.042 | 2.1(1.0-4.7) | 0.048 |
| >400 | 16/17 | 94.1 | 14.3(1.7-119.7) | 0.014 | 21.7(2.4-197.7) | 0.006 |
| *Smoking* | | | | | | |
| Yes | 7/9 | 77.8 | 1.6(0.3-7.7) | 0.580 | 1.4(0.2-9.0) | 0.707 |
| No | 183/265 | 69.1 | | | | |
| *Alcohol* | | | | | | |
| Yes | 48/74 | 64.9 | 0.8(0.4-1.3) | 0.329 | 0.9(0.5-1.7) | 0.774 |
| No | 142/200 | 71.0 | | | | |
| *Exercise* | | | | | | |
| No | 54/93 | 58.1 | | | | |
| Yes | 136/181 | 75.1 | 2.2(1.3-3.7) | 0.004 | 2.0(1.1-3.6) | 0.023 |
| *Body weight* | | | | | | |
| Underweight | 12/15 | 80.0 | 2.3(0.6-8.9) | 0.220 | 2.3(0.6-9.4) | 0.249 |
| Normal | 50/79 | 63.3 | | | | |
| Overweight | 87/137 | 63.5 | 1.0(0.6-1.8) | 0.975 | 0.7(0.4-1.3) | 0.240 |
| Obese | 41/43 | 95.3 | 11.9(2.7-52.8) | 0.001 | 10.4(2.3-47.6) | 0.003 |

**Number of subjects with SD/number of subjects in each category*

**Table 4.7 Rate of sexual dysfunction according to perceived intra-vaginal ejaculatory latency time, testosterone and glycated haemoglobin**

| Variables | n/N* | Rate of SD (%) | OR(95% CI | P value | aOR(95% CI | P value |
|---|---|---|---|---|---|---|
| *Adequate* | | | | | | |
| Low | 1/1 | 100 | NA | | NA | |
| Normal | 100/144 | 69.4 | | | | |
| High | 89/129 | 69.0 | 1.0(0.6-1.6) | 1.000 | 0.4(0.2-1.2) | 0.121 |
| *Desirable* | | | | | | |
| Low | 85/125 | 68.0 | 1.1(0.6-1.8) | 0.787 | 1.4(0.8-2.5) | 0.296 |
| Normal | 85/128 | 66.4 | | | | |
| High | 20/21 | 95.2 | 10.1(1.3-77.9) | 0.026 | 4.1(1.1-41.3) | 0.038 |
| *Too short* | | | | | | |
| Low | 25/37 | 67.6 | 1.1(0.5-2.2) | 0.870 | 1.1(0.4-2.5) | 0.893 |
| Normal | 139/210 | 66.2 | | | | |
| High | 26/27 | 96.3 | 13.3(1.8-99.9) | 0.012 | 8.2(1.0-74.1) | 0.040 |
| *Too long* | | | | | | |
| Low | 3/3 | 100.0 | NA | | NA | |
| Normal | 174/257 | 67.7 | | | | |
| High | 13/14 | 92.9 | 6.2(0.8-48.2) | 0.081 | 2.3(0.2-26.7) | 0.500 |
| *Testosterone* | | | | | | |
| Low | 6/12 | 50.0 | 0.4(0.1-1.3) | 0.122 | 0.3(0.1-1.2) | 0.077 |
| Normal | 161/225 | 71.6 | | | | |
| High | 23/37 | 62.2 | 0.7(0.3-1.3) | 0.249 | 0.9(0.4-2.0) | 0.775 |
| *HbA1c* | | | | | | |
| Normal | 17/27 | 63.0 | | | | |
| High | 173/247 | 70.0 | 1.4(0.6-3.1) | 0.450 | 1.0(0.4-2.6) | 0.947 |

**Number of subjects with SD/number of subjects in each category*

### *4.3.4 Perception of IELT*

The questions of primary interest in the measurement of perceived IELT involved respondent's definitions of "adequate" and "desirable" IELTs. The mean ± SD for these variables were, respectively, 8.2 ± 4.7 and 8.5 ± 4.9 minutes, with interquartile ranges (IQRs), respectively, of 5.0 to 10.0 (median = 7.0) and 5.0 to 10.0 (median = 8.0) minutes. (The IQR represents the responses of the middle 50% of respondents, the range from the 25th percentile to the 75th percentile of responses). The respondents were also asked the definitions for IELTs that were "too short" or "too long". The mean ± SD for these were, respectively, 1.6 ± 1.4 and 24.2 ± 10.9 minutes; IQRs for these variables were, respectively, 1.0 to 2.0 (median = 1.0) and 15.0 to 30.0 (median = 30.0) minutes (Table 4.5). However, when the perceived IELT were classified based on SD, those with SD significantly perceived higher time as being "adequate" (8.8 ± 5.3 min.), "desirable" (9.1 ± 5.6 min.) and "too short" (1.7 ± 1.5 min.) as compared to those without SD (7.4 ± 2.5, 7.7 ± 2.6 and 1.3 ± 0.7 for "adequate", "desirable" and "too short" respectively) (Table 4.5).

Overall, about half of the studied population perceived "adequate" and "desirable" IELT to last for 3-7 and 7-13 minutes respectively, while about 80% and 90% perceived "too short" and "too long" IELT to last 1-2 and 10-30 minutes respectively. About 47%, 8%, 10% and 5% perceived "adequate", "desirable", "too short" and "too long" IELT to last more than 7, 13, 2 and 30 minutes respectively (Table 4.8). When the perception was stratified based on sexual function, higher proportion of those with SD think that more than 13 minutes, 2 minutes and more than 30 minutes as being desirable (10.5%), too short (13.7%) and too long (6.8%) IELT respectively compared to 1.2% each for desirable, too short and too long among those without SD. Conversely, significantly lower proportion of those with SD perceived too short and too long IELT to last 1-2 minutes and 10-30 minutes respectively (Table 4.8).

**Table 4.8 Prevalence of abnormal perception of intra-vaginal ejaculatory latency, testosterone and glycated haemoglobin stratified by sexual dysfunction**

| Variables | Total (n=274) | NSD (n=84) | SD (n=190) | P value |
|---|---|---|---|---|
| ***Adequate (3-7)*** | | | | |
| Low | 1(0.4%) | 0(0.0%) | 1(0.5%) | 0.5053 |
| Normal | 144(52.6%) | 44(52.4%) | 100(52.6%) | 0.9694 |
| High | 129(47.1%) | 40(47.6%) | 89(46.8%) | 0.9054 |
| ***Desirable (7-13)*** | | | | |
| Low | 125(45.6%) | 40(47.6%) | 85(44.7%) | 0.6587 |
| Normal | 128(46.7%) | 43(47.1%) | 85(44.7%) | 0.3235 |
| High | 21(7.7%) | 1(1.2%) | 20(10.5%) | 0.0074 |
| ***Too short (1-2)*** | | | | |
| Low | 37(13.5%) | 12(14.3%) | 25(13.2%) | 0.8012 |
| Normal | 210(76.6%) | 71(84.5%) | 139(73.2%) | 0.0403 |
| High | 27(9.9%) | 1(1.2%) | 26(13.7%) | 0.0014 |
| ***Too long (10-30)*** | | | | |
| Low | 3(1.1%) | 0(0.0%) | 3(1.6%) | 0.2469 |
| Normal | 257(93.8%) | 83(98.8%) | 174(91.6%) | 0.0222 |
| High | 14(5.1%) | 1(1.2%) | 13(6.8%) | 0.0501 |
| ***Testosterone (2.25-9.72)*** | | | | |
| Low | 12(4.4%) | 6(7.1%) | 6(5.1%) | 0.1372 |
| Normal | 230(83%) | 66(78.6) | 164(86.3) | 0.1074 |
| High | 32(11.7%) | 12(14.3%) | 20(10.5%) | 0.3717 |
| ***HbA1c (3-6)*** | | | | |
| Low | 0(0.0%) | 0(0.0%) | 0(0.0%) | NA |
| Normal | 27(9.9%) | 10(11.9%) | 17(8.9%) | 0.4489 |
| High | 247(90.1%) | 74(88.1%) | 173(91.1%) | 0.4489 |

### 4.3.5 *Relationships between SD, IELT, anthropometric and biochemical variables*

Age generally associate positively with SD as well as its subscales. For the purpose of interpretation, Cohen (Cohen, 1977) considered $0.10<r<0.30$ as small, $0.30<r<0.50$ as medium and $r>0.50$ as large. SD increase with increase income level, greater perception of desirable and too short IELT. The degree of impotency also increase with increased income level, increased exercise level, increased perception of adequate, desirable, too short IELT and decreased testosterone level. Premature ejaculation is directly linked with increased exercise and higher perception of too short IELT in this study (Table 4.9). Non-sensuality correlate positively with income level, desirable and too short IELT whilst avoidance is positively associated with smoking and FBG but negatively with higher perception of "adequate", "desirable" and "too long" IELT. The lower the levels of sexual satisfaction from this study the higher the perception of "adequate", "desirable" and "too short" IELT. Non-communication is positively linked with income levels and higher perceptions of what was "adequate" IELT (Table 4.9).

**Table 4.9 Partial correlation between sexual dysfunction parameters and socio-demographic data, perceived intra-vaginal ejaculation latency time, as well as biochemical data**

| Variables | SD | IMP | PE | NS | AV | DIS | NC | INF |
|---|---|---|---|---|---|---|---|---|
| Age | **0.39*** ** | **0.31*** ** | **0.33*** ** | **0.39*** ** | 0.15** | 0.24*** | 0.21*** | 0.06 |
| Education | -0.04 | 0.10 | -0.07 | -0.09 | -0.07 | 0.05 | 0.05 | 0.00 |
| Income level | 0.20** | 0.21*** | 0.10 | 0.15* | -0.02 | 0.05 | 0.13* | 0.03 |
| Smoking | 0.04 | -0.09 | 0.04 | 0.00 | 0.15* | -0.01 | -0.02 | 0.10 |
| Alcohol | -0.03 | -0.03 | -0.09 | 0.00 | 0.09 | 0.02 | -0.05 | 0.03 |
| Exercise | 0.08 | 0.12** | 0.13* | 0.06 | -0.08 | 0.02 | -0.03 | -0.06 |
| Adequate | 0.10 | 0.15** | 0.03 | 0.07 | -0.13* | 0.16** | 0.15* | -0.07 |
| Desirable | 0.13* | 0.19** | 0.08 | 0.13* | -0.15* | 0.15** | 0.03 | -0.10 |
| Too short | 0.16** | 0.17** | 0.13* | 0.16** | -0.11 | 0.20** | 0.02 | -0.07 |
| Too long | -0.09 | 0.00 | -0.08 | 0.00 | -0.19** | -0.06 | 0.02 | -0.09 |
| BMI | 0.01 | 0.07 | -0.04 | -0.07 | 0.02 | -0.09 | -0.01 | 0.02 |
| FBG | 0.06 | 0.05 | 0.04 | 0.04 | 0.16** | -0.07 | 0.00 | 0.09 |
| Testosterone | 0.05 | -0.14* | 0.01 | 0.09 | -0.03 | 0.06 | 0.09 | 0.00 |
| HbA1c | 0.00 | 0.06 | -0.04 | -0.06 | 0.07 | 0.06 | 0.04 | 0.05 |

***Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed), ***Correlation is significant at the 0.001 level (2-tailed). Boldface r = Pearson product moment correlation coefficient with a medium size ($0.30 \leq r \geq 0.50$) effect.**

As shown in Table 4.10, testosterone correlates negatively with HbA1c, FBG, perceived desirable, too short IELT, and weight as well as waist circumference. Glycated haemoglobin correlates positively with perceived adequate, desirable, too long IELT and FBG. The older the study participant, the lower the income level, exercise level, perceived adequate, desirable IELT and FBG but the higher the WC. Those with higher educational level had higher income level, smoked less cigarette and perceived less time as being too short IELT. Cigarette also correlates positively with alcohol consumption. The perception of IELT as well as markers of obesity correlates positively with each other with a small to a large size effect (Table 4.10).

Generally, SD is linked positively with all the subscales. The subscales are also related positively with each other except for a negative association between premature ejaculation and avoidance as well as between avoidance and non-communication (Table 4.11).

**Table 4.10 Pearson Product Moment Correlation Coefficient between biochemical, socio-demographic and perceived IELT**

| Variables | HbA1c | Age | Edu | Income | Smk | Alc | Exr | Adeq. | Des. | TS | TL | WT | BMI | WC | WHR | FBG |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Testosterone | -0.12* | 0.07 | -0.08 | -0.02 | -0.09 | -0.07 | -0.09 | -0.11 | -0.12* | -0.16* | -0.06 | 0.23*** | 0.02 | -0.14* | -0.05 | -0.12* |
| HbA1c | | 0.07 | -0.02 | -0.07 | -0.04 | -0.06 | -0.10 | 0.18** | 0.13* | -0.01 | 0.17** | -0.03 | 0.03 | -0.04 | 0.02 | **0.31*** ** |
| Age | | | 0.02 | -0.16** | 0.06 | -0.06 | 0.14* | -0.15* | 0.21*** | -0.11 | -0.09 | -0.10 | 0.06 | 0.14* | 0.02 | -0.21*** |
| Education (Edu) | | | | 0.24*** | 0.16** | -0.03 | 0.07 | -0.05 | -0.09 | -0.17** | -0.04 | 0.07 | 0.03 | 0.08 | -0.02 | 0.02 |
| Income | | | | | 0.05 | -0.07 | 0.02 | -0.02 | -0.01 | 0.00 | -0.07 | 0.04 | 0.00 | -0.01 | -0.03 | -0.02 |
| Smoking (Smk) | | | | | | 0.14* | -0.04 | -0.05 | -0.05 | -0.04 | -0.08 | -0.04 | -0.01 | -0.04 | -0.01 | 0.02 |
| Alcohol (Alc) | | | | | | | 0.00 | 0.09 | 0.04 | 0.00 | 0.03 | -0.03 | 0.03 | -0.09 | -0.05 | 0.03 |
| Exercise (Exr) | | | | | | | | -0.10 | -0.03 | -0.02 | -0.10 | 0.18** | -0.01 | 0.02 | 0.00 | -0.20*** |
| Adequate (Adeq.) | | | | | | | | | **0.83*** ** | **0.63*** ** | **0.60*** ** | 0.15* | 0.02 | 0.06 | -0.05 | 0.03 |
| Desirable (Des.) | | | | | | | | | | **0.73*** ** | **0.66*** ** | 0.21*** | 0.04 | 0.07 | -0.04 | -0.02 |
| Too short (TS) | | | | | | | | | | | **0.34*** ** | 0.16* | 0.05 | 0.09 | -0.05 | -0.09 |
| Too long (TL) | | | | | | | | | | | | 0.12 | 0.06 | 0.03 | 0.00 | -0.05 |
| Weight (WT) | | | | | | | | | | | | | 0.15* | **0.42*** ** | -0.01 | -0.17** |
| Body mass index (BMI) | | | | | | | | | | | | | | **0.43*** ** | -0.01 | -0.08 |
| Waist circumference (WC) | | | | | | | | | | | | | | | 0.01 | -0.09 |
| Waist to Hip Ratio (WHR) | | | | | | | | | | | | | | | | 0.02 |

***Correlation is significant at the 0.05 level (2-tailed), **Correlation is significant at the 0.01 level (2-tailed), ***Correlation is significant at the 0.001 level (2-tailed). Boldface r = Pearson product moment correlation coefficient with a medium size ($0.30 \leq r \geq 0.50$) effect: boldface and underline *r* = Pearson product moment correlation coefficient with a large size ($r > 0.50$) effect.**

**Table 4.11 Pearson Product Moment Correlation Coefficient between sexual dysfunction including the 7 subscales of the GRISS**

| Variables | IMP | PE | NS | AV | DIS | NC | INF |
|---|---|---|---|---|---|---|---|
| Sexual dysfunction | **0.76*** ** | **0.69*** ** | **0.74*** ** | 0.14* | **0.63*** ** | **0.62*** ** | 0.16** |
| Impotence (IMP) | | **0.46*** ** | **0.54*** ** | -0.04 | **0.49*** ** | **0.39*** ** | -0.01 |
| Premature ejaculation (PE) | | | **0.54*** ** | -0.18** | **0.38*** ** | **0.37*** ** | -0.06 |
| Non-sensuality (NS) | | | | -0.09 | 0.44*** | **0.47*** ** | -0.10 |
| Avoidance (AV) | | | | | -0.02 | -0.13* | 0.25*** |
| Dissatisfaction (DIS) | | | | | | **0.39*** ** | 0.02 |
| Non-communication (NC) | | | | | | | 0.01 |

***Correlation is** significant at the **0.05 level (2-tailed),** **Correlation is significant at the 0.01 level (2-tailed), ***Correlation is significant at the 0.001 level (2-tailed). **Boldface** r = Pearson product moment correlation coefficient with a **medium size** ($0.30 \leq r \geq 0.50$) **effect: boldface and underline** *r* = Pearson product moment correlation coefficient with a large size ($r > 0.50$) effect, **INF** = Infrequency.

# *Chapter 5*

# DISCUSSION

## 5.1 INFLUENCE OF METABOLIC SYNDROME ON SD AMONG DIABETIC PATIENTS

The finding that subjects with SD were significantly older and with longer years (duration) of diabetes is consistent with the report of Jamieson *et al.*, (2008) in a survey of diabetics, they indicated that duration of diabetes, age, glycaemic control (HbA1c), weight, hypertension and microalbuminuria are the significant predictors of ED. It is possible that the duration of diabetes could represent the period it takes for atherosclerotic deposits in the microvascular system to reach a significant size in order to cause endothelial and erectile problems.

The prevalence of MetS amongst subjects with SD was 80%, 44.2% and 52.1% by the WHO,NCEP ATP III, and IDF criteria and this findings is consistent with previous evidence by Bansal *et al.*, (2005) who reported that out of 154 men with organic ED 90.9% displayed both IR and MetS. Corona *et al.* ,(2006) also reported that 96.5% of their subjects with MetS exhibited ED. Even though there was generally higher prevalence of MetS in subjects with SD compared to subjects without SD this difference did not reach a level of significance, this could be due to the fact that all subjects were diabetics and therefore all were significantly susceptible to the development of endothelial dysfunction and since both SD and MetS is thought to be mediated by endothelial dysfunction it is not surprising that a significant difference was not attained. A previous study in Kumasi on the prevalence of the MetS among diabetics established a rate of about 55.9% (Titty et al., 2008).

However Subjects with SD were seen to have significantly higher Systolic (SBP), Diastolic blood pressure(DBP), weight and BMI, and these are consistent with findings by Zhody *et al.*, (2007) in which the relationship between androgen deficiency, ED and MetS was established by analyzing BMI measurements in 158 obese men. They found a significant statistical association between increasing BMI with, systolic blood pressure, TGs, HDL, and LDL.

Even though subjects with SD had generally elevated levels of MetS parameters than subjects without SD only raised blood pressure (HBP), SBP, DBP attained significant differences. This finding is however consistent with evidence presented by Paick *et al.*, (2007) in which they did not find a significant relationship between ED severity and MetS parameters, except hypertension, in impotent men and they suggested that the relationship between MetS and ED may be selective for certain components. About 76.8% of subjects with SD in this study had increased blood pressure whilst 64.3% of subjects without SD had hypertension. This is in agreement with reports by Bener *et al.*, (2007) who reported that 66.2% of participants with hypertension reported erectile dysfunction whilst 23.8% of the non hypertensive participants had erectile dysfunction. It is possible that increased sympathetic tone in HBP combined with endothelial dysfunction in MetS, or other organic status, were the most plausible pathway for inducing ED.

When the components of the MetS was stratified based on sexual function only hypertension and obesity reached significant levels this could explain the complexity of the relationship between MetS and SD. It is therefore difficult to tell from this study whether MetS was the cause of SD or SD was causing the MetS.

What can be said from this study is the fact that endothelial dysfunction coupled with vascular disease is a very strong link between SD and MetS. Evidence of this is provided in Table 4.1 in which a strong association between SD and MetS components (all definitions) is clearly manifested. Androgen deficiency is a central component in the linkage between these two conditions and this is also shown by the negative association between testosterone levels and ED as well as the significantly lower testosterone concentration amongst subjects with SD.



## 5.2 DETERMINANTS OF SD AMONG DIABETIC PATIENTS

According to the World Health Organization, SD is defined as "the various ways in which an individual is unable to participate in a sexual relationship as he or she would wish". Diabetes mellitus could lead to multiple medical (DCCT Research Group, 1993), psychological (Ryan, 1997), and sexual (Thomas and LoPiccolo, 1994) dysfunctions. Reduced sexual function is a well-documented complication of diabetes. Previous reports have shown that diabetic men are at increased risk for SD at an earlier age (Feldman *et al.*, 1994; Webster, 1994; Close and Ryder, 1995; Fedele *et al.*, 2000), with an incidence ranging from 20% to 85% (Feldman *et al.*, 1994; Romeo *et al.*, 2000; Jones and Gingell, 2002). Most of the risk factors for SD (such as vascular disease, hypertension, peripheral neuropathy and obesity) overlap with many of the comorbidities linked with diabetes with prevalence and severity being more common in people with diabetes than in the general population (Jackson *et al.*, 2002).

The 69.3% rate of SD observed among this cohort of diabetic men was higher than the 66% reported among the general Ghanaian male population (Amidu *et al.*, 2010a), 59.8% reported among Ghanaian men with various medical conditions (Amidu *et al.*, 2010b) and the 59.2% reported among men in a marriage relationship

(Amidu *et al.*, 2011). However, this figure (69.3%) is in agreement with the 70.0% reported among self-reported diabetic subjects (Amidu *et al.*, 2010b). The agreement between the SD rate among self-reported and the clinically diagnosed diabetics in this study is reasonable since it can be assumed that subjects who reported that they were 'diabetic' did so on the basis of medical diagnosis. In all these studies, SD rate increased with age. High rate of SD among diabetic subjects could be due to the fact that, as part of the complications associated with diabetes, there is damage to small arteries and arterioles which could impair endothelium-dependent relaxation of penile smooth muscle thus preventing optimal blood flow to and from the penis, and maintenance of an erection (Eardley, 2002; Jackson *et al.*, 2002). Further research will however be required in Ghana to determine the prevalence rate of SD among type 1 and 2 diabetics and whether there are any differences in their association with SD.



In contrast, the 69.3% is higher than the 37% reported among Hong Kong diabetic men (Fedele *et al.*, 2000) but agrees with the 63.6% reported among Chinese diabetic men (Siu *et al.*, 2001) and the 20% to 85% incidence rate for diabetic subjects (Feldman *et al.*, 1994; Romeo *et al.*, 2000; Jones and Gingell, 2002) reported in other studies. This wide variation in the incidence of SD could be due in part to the definition used for SD, the period of data retrieval, the population surveyed, the setting in which the patients were studied, the manner in which the participants were questioned, the number and selection of participants, cultural background, socioeconomic level, quality of psychosexual relationships and income. Apart from these, the degree to which a medical condition and perceptual differences would affect SD is not known.

The observed higher perception of what is "adequate", "desirable" and "too short" IELT among those with SD from this study coupled with the positive association of

perceived IELT with SD, impotence, premature ejaculation and dissatisfaction means that these groups of diabetic men are unable to satisfy their sexual needs probably due to their erroneous perception of IELT. The innate standards as well as belief of an individual as modified by the type of formal and informal education received from the society, including pornographic movies could affect his /her quality of life and leads to distress and displeasure. Since stereotype and not reality is the main determinant of expectation (Miller and Byers, 2004), dissatisfaction due to wrong perception may ultimately lead to the purchase of performance enhancing medication even when such an individual does not actually need it, as observed currently among Ghanaian men. Care should be taken not to diagnose these groups of men as having PE. Recently, men who are not satisfied with their IELT while having a normal or even long IELT duration, have been classified as Premature-like Ejaculatory Dysfunction (Waldinger and Schweitzer, 2008). According to Waldinger et al., (2008) this PE subtype has a clearly different aetiology and pathogenesis than lifelong PE or acquired PE. These Ghanaian cohorts of men are most likely among the group of men who have Premature-like Ejaculatory Dysfunction.



The intersection between perceived "adequate" (5.0 to 10.0 minutes) and "desirable" (5.0 to 10.0 minutes) IELT means that an IELT of 5 to 10 minutes is perceived by respondents as normal. From this study, there is positive association between the perceived "too short" IELT and PE. For those who are dissatisfied with their ejaculation time, it may be erroneously classified as premature ejaculation, when their actual ejaculation time is less than their desirable IELT or the IELT that is generally considered as adequate in this population. The significant direct effect of perceived IELT with the level of dissatisfaction with sexual intercourse is in agreement in part with the finding of Patrick *et al.*,( 2007) who reported that, IELT has a significant direct effect on perceived control over

ejaculation, but not a significant direct effect on ejaculation-related personal distress or satisfaction with sexual intercourse. Self-estimated IELT is normally adequate for assessing PE in everyday clinical practice despite the fact that self-estimated and stopwatch-measured IELT are interchangeable and correctly assigned PE status with 80% sensitivity and 80% specificity (Rosen *et al.*, 2007).

The higher perception of "desirable" and "too short" IELT being a predictor of SD could account for the high rate of SD amongst subjects with higher expectations, thus further education and sensitization is needed to educate people on what adequate and too short IELT entails. This will go a long way to ease expectations, restore confidence and eventually eliminate inadequacy and gradually restore sexual function to normalcy. The boom of advertisement of sex enhancing drugs in the media does not help the situation and people are made to feel that sexual longevity is necessary to satisfy their partners and thus establishing a vicious cycle of inadequacy, lower perceptions of performance and eventually SD.

Several studies have demonstrated SD in diabetic populations, but the nature of the sexual complaints among this group is limited mainly to erectile dysfunction. As indicated by the GRISS, it appears that SD in this study is mainly related to infrequency (79.2%), non-sensuality (74.5%), dissatisfaction with sexual acts (71.9%), non-communication (70.8%) and impotence (67.9%). Other areas of sexual function, including premature ejaculation (56.6%) and avoidance (42.7%) were also substantially affected. However, severe SD was seen in 4.7% of the studied population. Also the most prevalent areas of severe difficulty were impotence (14.2%), avoidance (10.9%), premature ejaculation (8.8%), non-sensuality (7.3%), infrequency (4.0%), dissatisfaction (3.6%) and non-communication (3.3%).

The reduction in testosterone level among the participants with SD is in agreement with previous reports (Haffner *et al.*, 1997; Oh *et al.*, 2002; Selvin *et al.*, 2007;

Grossmann *et al.*, 2008). Testosterone could enhance copulation via increases in dopamine release in the medial preoptic area, perhaps through up-regulation of NO synthesis (Hull *et al.*, 1997; Hull and Dominguez, 2007). Androgens have long been implicated in the regulation of sexual behavior in the human male (Mooradian *et al.*, 1987). Higher testosterone levels could shorten the latency of erection activated by the introduction to sexual stimuli (Lange *et al.*, 1980), and testosterone substitution in hypogonadal males rejuvenates sexual interest, decreases latency, and increases frequency and enormity of nocturnal penile tumescence (NPT) (Kwan *et al.*, 1983). Available data also support the negative association of testosterone with markers of glycaemic control and obesity as shown by this study (Seidell *et al.*, 1990; Pasquali *et al.*, 1997; Svartberg *et al.*, 2004a; Svartberg *et al.*, 2004b; Osuna *et al.*, 2006). Increase in visceral, central or abdominal adiposity as measured by WC and possibly weight can lead to endocrinologic imbalances. These have been shown to relate positively with insulin, glucose levels and negatively with testosterone levels (Seidell *et al.*, 1990). This study is also in agreement with the assertion that WC should be the preferred anthropometric variables in predicting endogenous testosterone level (Seidell *et al.*, 1990; Pasquali *et al.*, 1997; Svartberg *et al.*, 2004a; Svartberg *et al.*, 2004b; Osuna *et al.*, 2006). The mechanism could be due in part to increase in serum leptin level production (Isidori *et al.*, 1999) and/or excess cortisol secretion (Rosmond *et al.*, 2003) which mimic LH/hCG-stimulated androgen suppressing androgenic hormone formation.

From this study, it seems that higher level of education offer the participants' better job and income level. Participants with SD had higher income levels and were heavier as compared to those without sexual dysfunction. High income and obesity were found to be risk factors for SD from this study. It is not very surprising to find this phenomenon in Africa (at least in Ghana) because the higher class of African societies with higher income levels are known to be the major

consumers of junk food as well as alcohol and in developing stress free lifestyles which are basically sedentary, whilst the poor and low income earners struggle to feed well and are exposed to strenuous activity. Even though obesity was not a significant risk factor for SD in a previous report among the general male populace as well as those with various medical conditions (Amidu *et al.*, 2010a; Amidu *et al.*, 2010b), it could mean that the impact of obesity on the sexual function of the diabetic patient is different from that observed among non-diabetic subjects. Obesity is associated with a state of chronic oxidative stress and inflammation (Higdon and Frei, 2003) leading to the impairment of endothelial function resulting in SD and laying the ground work for atherosclerosis (Fonseca and Jawa, 2005). Since atherosclerosis of the arteries supplying genital tissues greatly affects sexual function, it seems rational to assume that conditions predisposing to atherosclerosis (diabetes, obesity) might impair sexual function.

Reported literature indicates a decreased relative risk of developing SD with increased physical activity (Bacon *et al.*, 2003; Esposito *et al.*, 2004). Whether this reduced risk applies to diabetic men is not known. Exercise from this study was a significant risk factor even after adjustment for age, income levels and obesity. This finding is contrary to a previous report among the general male population of Ghana (Amidu *et al.*, 2010a) and among men with various medical conditions (Amidu *et al.*, 2010b) where exercise was not a significant risk factor for SD. Reasons for this disparity is not readily known from this study, however, in a follow-up study by Derby *et al.*, (2000), overweight men at baseline were found to be at an increased risk of developing SD regardless of whether they lost weight.

Even though exercise is a key aspect of a healthy lifestyle, strenuous physical exercise results in increased oxygen consumption, increased metabolism and increased production of reactive oxygen species which would ultimately lead to oxidative stress (George and Osharechiren, 2009). Diabetes has also been thought

to be mediated by oxidative stress as the underlying mechanism. Thus as diabetics exercise they confound their oxidative stress levels and this will eventually worsen their health and cause sexual dysfunction. There is therefore the need for further study to define the level of exercise needed by diabetic patients for effective glycaemic control and also to prevent oxidative stress induced SD.



# *Chapter 6*

# CONCLUSIONS AND RECOMMENDATIONS

## 6.1 CONCLUSIONS

The prevalence of MetS as defined by the various criteria was 78.8%, 43.4% and 51.8% for WHO, NCEP ATP III and IDF respectively. There was a significantly positive association of SD with blood pressure and the duration of diabetes which implies the worsening of SD once a subject had hypertension and had a longer duration of diabetes.

The prevalence of SD (69.3%) among these diabetic patients is high but similar to that reported among self-reported diabetic patients (70.0%) in Kumasi, Ghana and correlates positively with age, income level and perceived desirable and too short IELT. The determinants of SD from this study are income level, exercise, obesity, higher perception of "desirable" and "too short" IELT. The perceived "adequate", "desirable", "too short" and "too long IELT are 5-10, 5-10, 1-2 and 15-30 minutes respectively. This could impact significantly on the individual's self-esteem and quality of life thereby causing emotional distress leading to relationship problems.

## 6.2 RECOMMENDATION

It was not possible to determine from this study whether MetS was the cause of SD or vice versa and as such would warrant further investigation. Further research will however be required in Ghana to determine the prevalence rate of SD among type 1 and 2 diabetics and whether there are any differences in their association with MetS.



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The sample size (n) was calculated using the following considerations.

The population size (N) of the Tema metropolis was 209,000 as at the 2000 census. The confidence interval was targeted at 90.0%.The desired margin of error (ME) was set at 0.05.The population proportion (P) was set at 50% (0.5)

$$n = \frac{X^2 * N * P * (1-P)}{(ME^2 * (N-1)) + (X^2 * P * (1-P))}$$

Where:

n = sample size

$X^2$ = Chi – square for the specified confidence level at 1 degree of freedom

N = Population Size

P = population proportion (.50 in this table)

ME = desired Margin of Error (expressed as a proportion)



n = 270

A sample size of 300 was targeted with expectation of few patients who might opt out of the research or have incomplete data.