THE PREVALENCE OF HYPOGONADISM AND ITS ASSOCIATION WITH DIABETES MELLITUS, HYPERTENSION, CARDIOVASCULAR DISEASE, OSTEOPOROSIS, FRAILTY AND OBESITY IN ELDERLY MEN ATTENDING GERIATRIC OPD AT A TERTIARY CARE CENTRE IN SOUTH INDIA

A DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF
M.D. GERIATRICS EXAMINATION OF
THE TAMIL NADU DR. M.G.R. UNIVERSITY, CHENNAI
TO BE HELD IN MAY 2022
Registration Number: 201826053

DECLARATION

This is to declare that this dissertation titled “The prevalence of hypogonadism and its association with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis, frailty and obesity in elderly men attending geriatric OPD at a tertiary care centre in south India” is my original work done under the guidance of Dr Gopinath Kango Gopal, in partial fulfilment of rules and regulations for MD Geriatrics examination of the Tamil Nadu Dr.M.G.R Medical University, Chennai to be held in May 2022. Any information taken from secondary sources has been given due acknowledgement and citation.

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CERTIFICATE I

This is to certify that the dissertation entitled “The prevalence of hypogonadism and its association with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis, frailty and obesity in elderly men attending geriatric OPD at a tertiary care centre in south India” is a bonafide work done by Dr. Raeba Eldhose carried out under our guidance, towards the partial fulfilment of rules and regulations for MD Geriatrics degree examination of the Tamil Nadu Dr. M.G.R Medical University, to be conducted in May 2022.

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LIST OF ABBREVIATIONS AND ACRONYMS:

OPD	Outpatient department
DEXA	Dual energy X-ray absorptiometry
ECG	Electrocardiogram
ISA	International Society of Andrology
ISSAM	The International Society for the Study of the Aging Male
EAU	European Association of Urology
SHBG	Sex hormone binding globulin
ISSM	International Society for Sexual Medicine
LOH	Late Onset Hypogonadism
HIM	hypogonadism in males
TT	Total testosterone
GNRH	Gonadotropin releasing hormone
HPT	Hypothalamus-pituitary-testis (HPT) axis
LH	Luteinizing hormone
BMI	Body Mass Index
AMS	Aging Males' Symptoms
ADAM	Androgen Deficiency in the Aging Male
MMAS	The Massachusetts Male Aging Study
NERI	New England Research Institute
AMS	The Aging Males' Symptoms (AMS)
EMAS	European Male Aging Study
AUA	American Urological Association
PSA	Prostate specific antigen
TRT	Testosterone replacement therapy
TSH	Thyroid stimulating hormone
IM	Intramuscular
SC	subcutaneous
DHT	Dihydrotestosterone
RCT	Randomized Controlled Trials
LUTs	Lower urinary tract symptoms
KNDY	kisspeptin/neurokinin B/dynorphin neurons
CVD	Cardiovascular disease
CRP	C-reactive protein
VCAM	Vascular Cell Adhesion Molecule
LM	total lean body mass
ASLT	appendicular lean soft tissue mass

BMD	Bone Mineral Density
FSH	Follicle stimulating hormone
GELDING	Gut Endotoxin Leading to a Decline IN Gonadal function
IRB	Institutional Review Board
BPH	benign prostate hyperplasia
IQR	interquartile range
SPSS	Statistical Package for Social Services
SGLT-2	sodium-glucose cotransporter-2
DPP	Dipeptidyl-peptidase
ACE	Angiotensin converting enzyme
ARB	Angiotensin receptor blocker
CI	Confidence Interval
OR	Odds Ratio

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AIMS AND OBJECTIVES

AIM

To find the prevalence of hypogonadism in elderly males attending Geriatrics OPD and to look for association of hypogonadism with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis, obesity and frailty.

OBJECTIVES

Primary objective: To identify the prevalence of hypogonadism in elderly men attending geriatric OPD

Secondary objective: To estimate the association of diabetes mellitus, hypertension, cardiovascular diseases, osteoporosis, frailty and obesity with hypogonadism.

INTRODUCTION

With the newer advances in health care, the life expectancy of people has been steadily increasing over the years. According to the latest WHO data published, life expectancy in India among males is 69 yrs and among females is 72 yrs . However, this means there is also a steady increase in diseases associated with aging. Diabetes Mellitus, Hypertension, cardiovascular diseases, osteoporosis, frailty and obesity are known to be higher in elderly. Hypogonadism also seems to be higher in elderly males.

Hypogonadism is diagnosed by a low testosterone concentration in serum and symptoms of decreased energy and libido. Hypogonadism in elderly males is usually overlooked. The prevalence of hypogonadism in elderly males was found to vary from 10.8% to 53% among different studies. The role of ethnicity, geographical region, lifestyle or comorbidities on the level of testosterone in elderly males is not clearly established. Many studies show that hypogonadism is associated with increase in mortality and morbidity. Various studies done has shown higher prevalence of diabetes mellitus, metabolic syndrome, cardiovascular disease, osteoporosis, obesity and frailty in males with hypogonadism. It is still not known whether hypogonadism is a risk factor or an outcome of these comorbidities. While it is a well-known fact that women attain menopause , it is still not known whether males have a particular age after which they become testosterone deficient. It is well established that oestrogen has a protective effect against metabolic syndromes, however there is still no consensus on whether testosterone has a protective or a detrimental association with metabolic syndromes. Upcoming studies , however indicate a protective association. This study aims to find the prevalence of hypogonadism in elderly males attending geriatric OPD for any indication. This study also aims to compare the two groups, namely, men with hypogonadism and those without hypogonadism on their association with diabetes, hypertension, cardiovascular disease, obesity, frailty and osteoporosis.

ABSTRACT

Background : Male hypogonadism is common in the elderly. Studies have shown a prevalence varying from 10.3%-53%. It is associated with higher prevalence of cardiovascular disease, hypertension, diabetes mellitus, osteoporosis, obesity and frailty. Since these are associated with high morbidity and mortality, identification of any new risk factor and its prevalence will be useful in taking steps for prevention of these diseases.

Aim : The aim of the this study was to find the prevalence of hypogonadism in elderly males attending geriatrics OPD and to look for association of hypogonadism with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis, obesity and frailty.

Setting and design : This cross sectional observational study was conducted in the Geriatric medicine OPD at Christian Medical College, Vellore.

Method: The blood samples of patients who present to geriatrics OPD for any indication was taken to assess for total testosterone levels till the sample size was obtained . Free and total testosterone levels were assessed in all the individuals. History of hypertension, diabetes mellitus, cardiovascular diseases were noted . ADAM questionnaire was asked and short physical performance battery was performed. Blood pressure, weight and height were also assessed. Fasting and post prandial glucose levels, ECG changes suggestive of ischemic heart diseases, DEXA scan were obtained from the investigations report of the patient. The prevalence of hypogonadism and the association of hypogonadism with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis, obesity and frailty were assessed. Analyses was done using Statistical Package for Social Services (SPSS) software Version 21.0 (Armonk, NY: IBM Corp) and R

Results : The criteria for hypogonadism in our study was a combination of symptoms of hypogonadism with a total testosterone <300ng/dL. The prevalence of hypogonadism in our study was 47%(n - 74). Total testosterone< 300ng/dL was found in 58% of the participants. When free testosterone <5 ng/dL was considered, the prevalence was even higher at 61%.

Age had a significant association with hypogonadism and free testosterone. However total testosterone, though it showed a downward trend, did not have a significant association with age.

Diabetes had a significant association with hypogonadism and total testosterone both on univariate and multivariate analysis, but was not significantly associated with free testosterone level. There was a significant association between BMI and total testosterone and hypogonadism . BMI was not associated with free testosterone. Frailty was significantly associated with free testosterone but not with total testosterone or hypogonadism. Cardiovascular disease did not have any significant association with hypogonadism, as well as total or free testosterone. On multivariate analysis, however cardiovascular disease had a significant association with free testosterone. We found that the prevalence of osteoporosis was low in those with low testosterone. This contradictory result was thought to be due to the effect BMI had on osteoporosis and total testosterone. Multivariate analysis done however showed osteoporosis had no association with hypogonadism, total testosterone or free testosterone. Hypertension also did not have any significant association with hypogonadism, total testosterone or free testosterone.

Adams questionnaire had a sensitivity of 79.57% and specificity of 18.18 % to detect total testosterone less than 300 ng/dl. Its sensitivity and specificity to detect free testosterone < 5 ng/dl was slightly higher at 80.41% and 19.35% respectively.

Conclusion: The prevalence of hypogonadism(Men with symptoms of hypogonadism along with total testosterone < 300 ng/dl) in our study was 47%(n - 74). 58% had Total testosterone < 300ng/dl

and 61% had free testosterone <5 ng/dl. Age, diabetes, obesity and dyslipidaemia had a significant association with hypogonadism(symptoms + testosterone < 300 ng/dl) while diabetes mellitus , BMI and dyslipidaemia had a significant inverse association with total testosterone. Free testosterone had a significant association with age, cardiovascular disease, ischemic heart disease and frailty.

REVIEW OF LITERATURE

HISTORY

The functions of the testes have been known since ancient times The active agent responsible for virility or manhood, that is testosterone has only been identified later. Nevertheless, it was always assumed that the testes contain the ingredients required for manhood. Organotherapy with animal testis and even testis transplantation have been used over many years in different medical cultures for treatment of symptoms of hypogonadism. Many anecdotes in historical literature suggests that surgeons were transplanting testes of humans and animals to patients with features of hypogonadism (1).

The search for the hormone responsible for male virility intensified in the early 1900s and in 1935 , Ernst Laqueur's team isolated testosterone from bull testes in Amsterdam. In the same year testosterone was chemically synthesized independently by Adolf Butenandt's team in Gottingen and Leopold Ruzicka's team in Basel(2)Since then testosterone has been available in various forms, including oral, intramuscular and transdermal preparations and it has been applied in health care .

DEFINITION

Hypogonadism is a condition characterized by diminished levels of sexual hormones in circulation. Hypogonadism in males is characterised by diminished levels of male sexual hormone , testosterone in circulation .

Late onset hypogonadism is considered a clinical and biochemical syndrome, characterised by low levels of testosterone in the serum and symptoms of testosterone deficiency(3). This is in

consistency with the ISA, ISSAM and EAU recommendations on the definition of hypogonadism(4).

The clinical symptoms of hypogonadism include(5):

(1) Reduced or diminished libido or sexual desire with decreased erectile quality. Nocturnal erections are particularly diminished.

(2) Changes in mood, concomitant decreases in intellectual activity, cognitive functions, spatial orientation ability and fatigue. Depressed mood and irritability are common.

(3) Sleep disturbances in the form of insomnia and in some cases, excessive sleep.

(4) Sarcopenia or decrease in lean body mass with associated diminution in muscle volume and strength

(5) Increase in visceral fat

(6) Decrease in body hair and skin alterations

(7) Decreased bone mineral density resulting in osteopenia, osteoporosis and increased risk of bone fractures.

The following biochemical investigations are also required(3) :

Between 07.00 and 11.00 hours , A serum sample for total testosterone determination and sex hormone binding globulin (SHBG) should be obtained. This time period is ideal as testosterone has diurnal variation . The parameters necessary for establishment of hypogonadism are serum total testosterone and serum free testosterone. Serum free testosterone is calculated from total testosterone and SHBG .

There are no generally accepted lower limits for normal testosterone. It is not clear whether geography and ethnicity play a role in the level of testosterone. Different societies and different studies have different cut off value for testosterone. Total testosterone below 300 ng/dl is considered

as cut off by the endocrine society (6)and the American urological association(7). They advise repeated morning testing of testosterone in the morning time before confirming the diagnosis. ISSAM (International Society for the Study of the Aging Male) (8)and ISSM(International Society for Sexual Medicine) (9)consider total testosterone levels of 12 nmol/L (346 ng/dl) or free testosterone levels of 250 pmol/L (72 pg/ml) as a cut off . Endocrine society and the American Urological Association consider a total testosterone less than 300 ng/dl as deficient(6). Based on studies in younger men , there is also a general consensus that serum total testosterone levels below 8 nmol/L (231ng/dl) or free testosterone below180 pmol/L (52 pg/ml) require substitution. Salivary testosterone has been found to be a reliable substitute for free testosterone measurements. However, it cannot be recommended at this time as the methodology has not been standardized and adult male ranges are not available in most hospital or reference laboratories.

EPIDEMIOLOGY

With latest advances in medical field, the life expectancy of our population is steadily increasing. The prevalence of late onset hypogonadism or hypogonadism that is seen in elderly males are also increasing day by day . The main challenge for identifying the prevalence of late onset hypogonadism is the absence of a proper diagnostic criteria. There is still no clear guidelines on cut off for testosterone to diagnose hypogonadism .

The largest study done on hypogonadism prevalence is the European ageing male study. The criteria used by this study for diagnosis of late onset hypogonadism was presence of three sexual symptoms (decreased sexual interest and morning erections and erectile dysfunction) in combination with total T below 11 nmol/litre(317 ng /dl) and free T below 220 pmol/litre. Men aged 40 -79 was included in this study. The prevalence of late onset hypogonadism was 2.1% (63 of 2966)according to this study. (10)In a national survey conducted in China, Free Testosterone level

of <210 pmol/L with the presence of at least three sexual symptoms were considered as the criteria to define late onset hypogonadism. Based on this criterion, the prevalence of LOH was 7.8% (395 of 5078 subjects)(11) . The HIM(hypogonadism in males) study considered a TT level less than 300 ng/dl or previously diagnosed hypogonadal and receiving androgen treatment as criteria for hypogonadism. It included men >45 years of age. It showed a prevalence of 38.7% (12). The prevalence of symptomatic androgen deficiency in men study included men between ages of 30 and 79 . Symptomatic androgen deficiency was defined as low total (<300 ng/dl) and free (<5 ng/dl) testosterone along with presence of low libido, erectile dysfunction, osteoporosis or fracture, or two or more of following symptoms: sleep disturbance, depressed mood, lethargy, or diminished physical performance. The prevalence was found to be 5.8 % according to this study(13) . There were only few studies in India that looks at prevalence of LOH . A study conducted by Yadav Et al. in India showed a prevalence of 28.99%(14). The varying percentages of prevalence of LOH in different parts of the world could be due to the different criteria used for diagnosis. The possibility of ethnicity and other environmental factors affecting the testosterone levels is another possibility to consider. A uniform definition and comparative studies and metanalysis need to be done to probe further into these . Whether a different cut off of testosterone is needed for different population needs to be reviewed .

Most of the studies uniformly found that as age increases, hypogonadism increases. Liu et al found that the prevalence of hypogonadism was 0.9% for men 40 years–44 years of age, 3.2% for those 50 years–54 years, 11.2% for those 60 years–64 years and 24.0% for those 75 years–79 years (11). Araujo et al found prevalence was low in men less than 70 yrs. (3.1–7.0%) and increased markedly with age to 18.4% among 70 yr. olds(13).

More than total testosterone, the free testosterone level was found to be steadily decreasing as age increases (11). However the free testosterone level was found to be not very useful if total testosterone was less than 8 nmol per litre(15).

The prevalence of late-onset hypogonadism also was showed a rising trend with an increase in the body-mass index and an increasing number of other coexisting illnesses.

PATHOPHYSIOLOGY

Testosterone production is regulated by hypothalamus, pituitary and the testes in male body. The hypothalamus secretes GNRH down the hypothalamo-hypophyseal portal system to the anterior pituitary, which secretes luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH and FSH are two gonadotropic hormones that travel through the blood circulation and act on receptors in the gonads. LH, in particular, acts on the Leydig cells in the testis to increase testosterone production. Production of testosterone is limited by a negative feedback. High levels of testosterone are detected by receptors in the hypothalamus and pituitary , thereby reducing the levels of GNRH and gonadotrophins respectively. (16)

The majority of testosterone produced is bound to plasma proteins such as sex-hormone-binding-globulin and albumin. This testosterone that is protein-bound , acts as a surplus supply of testosterone hormone for the body. The free testosterone, which is a very small amount is the active testosterone in male body .

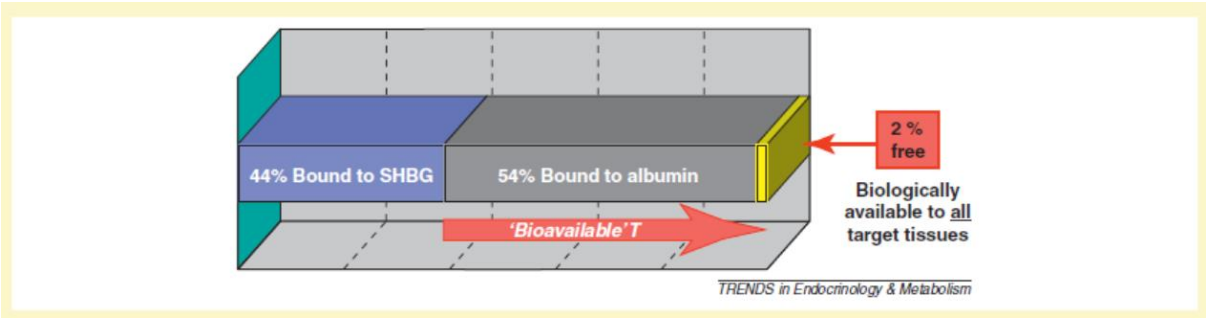


FIGURE 1. BOUND AND FREE TESTOSTERONE IN THE PLASMA (17)

Hypogonadism is a condition in which there is diminished levels of sexual hormones in the body. Male hypogonadism is characterised by low levels of male sexual hormone, testosterone in circulation .

Classically , male hypogonadism is classified as :

Primary(hypergonadotropic hypogonadism)) and

Secondary (hypogonadotropic Hypogonadism)

Primary hypogonadism is due to a testicular failure to produce Testosterone. In primary hypogonadism , due to feedback mechanism , the gonadotrophins are high . Hence the term hypergonadotropic hypogonadism.

Secondary hypogonadism is due to reduced levels of gonadotrophins which will result in low level of testosterone. There is a dysfunction of the hypothalamus-pituitary-testis (HPT) axis.

Late-onset hypogonadism (LOH) cannot be classified into either of the above . It has components of both primary and secondary hypogonadism .

Three main phenomena are described as the cause of late onset hypogonadism . They are :

1) A decline in testicular function

2) A decline in hypothalamic–pituitary function

3) A rise in the levels of sex-hormone-binding globulin

As age advances, testicular function declines slowly. However , purely age-related change is usually small and probably of the same magnitude as that of other organs of the body. This is in clear contrast to what happens to ovary in females , which undergoes a fast functional involution at menopause. Hence , we can’t form any parallels on the functional decline of testis from what is seen

in ovary of the females . Sufficient spermatogenesis remains upon ageing to maintain a man's fertility throughout his entire post-pubertal life. Testicular volume is a clear reflection of the quantity of sperm production, and it decreases by about 15% between the ages of 25 and 80–90 years.

Other changes seen are also seen with ageing . There is decrease in vascular supply to the testis with age and less responsiveness of the Leydig cells to luteinizing hormone . There is decrease in the production of seminal fluid . Sperm become less motile and their structure deteriorates. However, the sperm concentration in semen remains quite constant. As the age of the male partner increases, the time of unprotected intercourse needed to achieve fertilization, after correction for the woman's age, becomes longer and longer . The testis also undergoes morphological changes upon ageing including degeneration of the germinal epithelium and increased proportion of connective tissue. Also, the total number of Sertoli and Leydig cells in the testis decreases to around half of that of the young testis.(17)

The serum concentration of testosterone reaches its maximum at about 25–30 years of age and starts a slow steady decline thereafter at a rate of about 1% per year (18), (19). Another study found that , between 55 and 68 years of age , serum total testosterone decreases by 1.4% per year, free testosterone by 2.7%, while SHBG increases by 2.7%.(20). There is a great inter individual variability is in the aging-related decline of Testosterone. About 20% on men over 60 years have a serum testosterone in the upper normal range for young men, and about 20% being below the reference range. The bioavailable testosterone is in the subnormal range in a very large proportion of older men.

About half of circulating testosterone is bound to SHBG and another half to albumin. Protein bound testosterone is not biologically active. Only 0.5%–3% of testosterone remains in free,

non-protein-bound form and it is the only biologically active fraction(21). With ageing , the concentration of SHBG increases , which means more testosterone is bound to SHBG and lesser amount of testosterone is in the free biologically active form . This, in effect will cause a larger increase of free testosterone , by about 2%–3% per year even though the decline in total testosterone is not so much . Even with the age related decline in free testosterone, average free testosterone level still remains within the normal range in most men . In this situation , there is a reciprocal increase in luteinizing hormone (LH) secretion(22), (23).

The hypothalamo-pituitary function also shows a decline with age . The pulse frequency as well as the amplitude of secretion of gonadotrophins is reduced. This results in a lower level of stimulation of the testes to produce testosterone. Another complexity to the age-related changes in Testosterone is levels is caused by the associated weight gain and deterioration of general health due to chronic diseases such as diabetes, hypertension, cardiac, hepatic or renal failure, chronic obstructive lung disease and arthritis. The medications associated with these disorders, which include opiates and glucocorticoids, also contribute to the decreased Testosterone through actions on LH secretory dynamics. Testosterone production in a man can be considered a good indicator of his general health, which decreases in response to a variety of stressors. High body mass index (BMI) has a great suppressive effect on testosterone production and its effect is much greater than that of chronological age . There is almost a 30 % reduction in testosterone levels in a man with obesity(BMI > 30kg/m-2) when compared to a man with a BMI < 25 at any age. This is more than the purely age-dependent decrease between 40 and 80 years. The exact mechanism by which this happens is unknown, but it is thought to be linked to the increased negative feedback inhibition of gonadotropin secretion by adipose tissue-derived oestrogens, leptin and cytokines/adipokines(24), (25),(26). There is a similar decrease in testosterone associated with chronic illnesses. In men with

obesity and chronic illnesses, there is no increase in gonadotrophins. This points towards a secondary hypogonadism pathology in these cases.

Figure 2 shows a decrease in total testosterone and free testosterone with age and increase in LH and SHBG as age increases. (17)

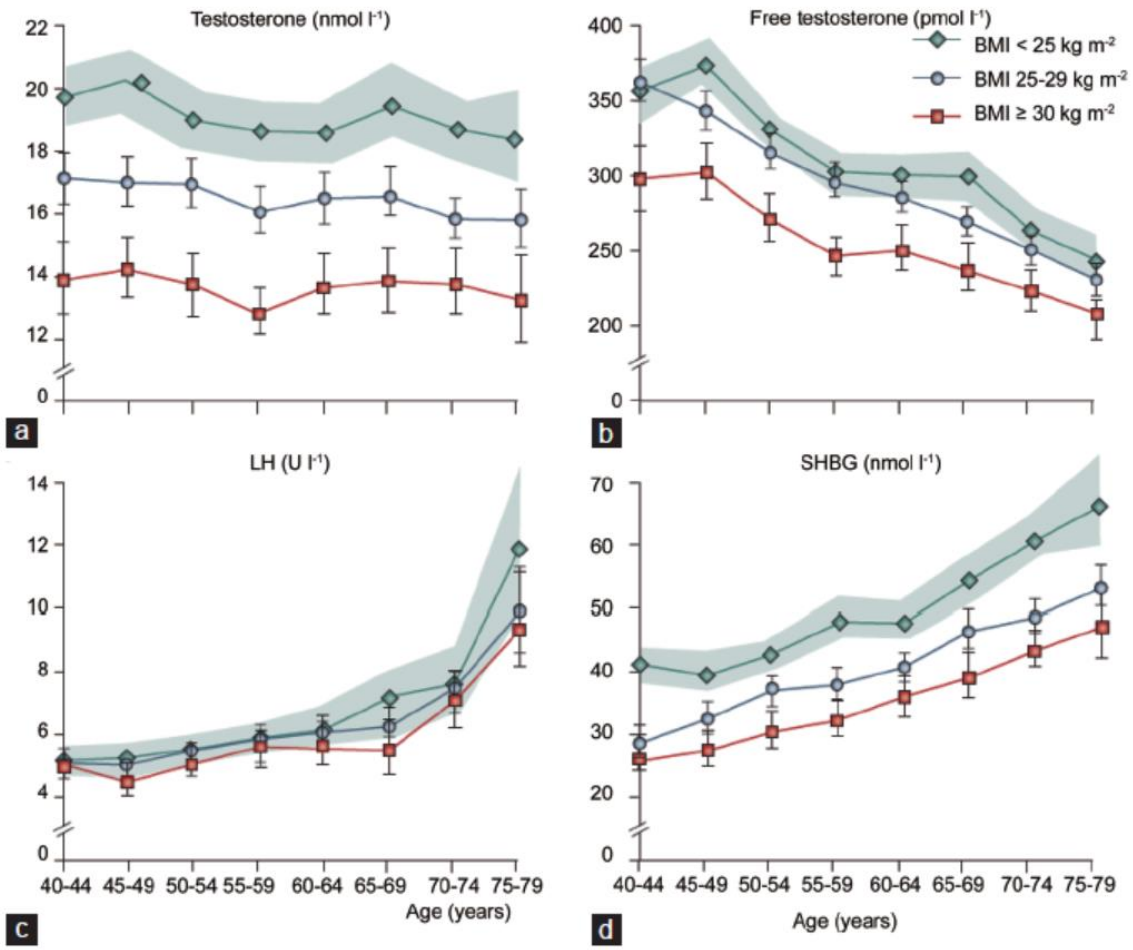


FIGURE 2: TESTOSTERONE, FREE TESTOSTERONE, LH AND SHBG LEVELS IN DIFFERENT AGES AND FOR DIFFERENT BMI(23)

DIAGNOSIS OF LATE ONSET HYPOGONADISM

Diagnosis of late onset hypogonadism is challenging and many cases go unrecognised. The symptoms of testosterone deficiency is insidious in onset and presents very subtly. Most of the times, patients and clinicians view it as an inevitable part of ageing.

Declining testosterone presents with multiple symptoms. It includes a gradual change in body composition, diminished energy and muscle strength, reduced sexual function with erectile dysfunction and reduced sexual interests, increased osteoporosis risk, anaemia, and changes in mood and cognitive ability (27), (28).

An understanding of the multiple functions of testosterone in a normal male is necessary to appreciate the effects that can be produced by the lack of testosterone. The table below shows the normal functions of testosterone:

TABLE 1: BIOLOGICAL ACTIONS OF TESTOSTERONE(29)

Stimulates synthesis of erythropoietin from kidneys for haematopoiesis
Maintaining normal muscle mass and metabolism by retaining nitrogen
Inhibits osteoclastic activity and enhances osteoblastic activity thereby stimulating bone mineralisation
Inhibits autoimmune rheumatic disease by inhibiting inflammatory response
Liver protein formation stimulation
Stabilise mood, reduces depression , irritability and improves self esteem
Enhances various cognitive parameters
Maintains frequency of nocturnal erections and at a lesser degree, volitional erections
Libido enhancement

SYMPTOMS

Symptoms that lead patients to clinic include: erectile dysfunction ,reduced libido or impotence, a reduction in muscle mass and strength or fatigue and lack of energy, a change in body composition in the form of an increase in visceral fat, osteoporotic changes, and change in mood and cognitive function. Other subtle and comparatively less frequently reported symptoms that can also be characteristic of LOH are: irritable feeling, anxiety, forgetfulness, disturbance in sleep, sweats and hot flushes, a decreased feeling of well-being, anaemia, hypertension, and regression in secondary sexual characteristics like a reduction in body hair and signs of atrophy of skin and ageing. As these

symptoms can be seen in other pathologies also, clinicians need to rule out other aetiologies before attributing the symptoms to hypogonadism.

Table 2 gives the key symptoms identified by ISSAM(International society for the study of the ageing male) in the ageing male that should alert suspicion of late onset hypogonadism.

TABLE 2: KEY SYMPTOMS THAT SHOULD RAISE SUSPICION OF LATE ONSET HYPOGONADISM(ISSAM) (28)

Diminished sexual desire and quality of erection, especially nocturnal erections
Mood changes associated with decrease in intellectual activity, ability for spatial orientation, depression, irritability and fatigue
Reduction in lean body mass with concomitant reduction in muscle mass and strength
Reduction in body hair and alteration in skin
Decreased mineralisation of bone hence causing osteopenia and osteoporosis
Increased visceral fat

The European association of urology suggests the following symptoms are associated with low testosterone.

TABLE 3: SYMPTOMS ASSOCIATED WITH LOW TESTOSTERONE (30)

Clinical symptoms and signs suggestive for androgen deficiency:
Reduced testis volume
Male-factor infertility
Decreased body hair
Gynaecomastia
Visceral obesity
Decrease in lean body mass and muscle strength
Metabolic syndrome
Insulin resistance and type 2 diabetes mellitus
Decrease in bone mineral density (osteoporosis) with low trauma fractures
Mild anaemia
Sexual symptoms:
Reduced sexual desire and sexual activity
Erectile dysfunction
Fewer and diminished nocturnal erections

Cognitive and psycho-vegetative symptoms:
Hot flushes
Changes in mood, fatigue and anger
Sleep disturbances
Depression
Diminished cognitive function

Studies have shown that various levels of testosterone in patients with late onset hypogonadism may be associated with different symptoms. Loss of libido and vigour may occur at testosterone levels below 15 nmol/L (433 ng/dl). Abdominal obesity is prevalent when testosterone levels are below 12 nmol/L(346 ng/dl) . Depressed mood, sleep disturbance, lack of concentration and diabetes mellitus type 2 are common when testosterone levels are below 10 nmol/L(288 ng/dl). Decreased frequency of sexual thoughts , hot flushes and erectile dysfunction were associated with testosterone levels below 8 nmol/L(231 ng /dl) (31). Three main sexual symptoms that is, decreased sexual thoughts, erectile dysfunction and weakened morning erections was the strongest predictor for hypogonadism in this age group (30). The strongest predictor of hypogonadism is a serum total testosterone level of < 8 nmol/L or serum testosterone in the range of 8-11 nmol/L and free testosterone < 220 pmol/L.(30)

PATIENT ASSESSMENT AND SCREENING QUESTIONNAIRES

Various screening tools have been validated for patients with suspected hypogonadism.

The Aging Males' Symptoms (AMS) scale

The ageing male symptoms scale in Europe, which was developed in 1999 captures symptoms that could suggest late onset hypogonadism.

***TABLE 4:THE AGING MALES' SYMPTOMS (AMS) SCALE – A VALIDATED QUESTIONNAIRE FOR ASSESSING THE SEVERITY AND IMPACT OF SYMPTOMS IN LATE-ONSET HYPOGONADISM*(32)**

	Symptoms	Score				
		1	2	3	4	5
1	Decline in your feeling of general well-being (general state of health, subjective feeling)					
2	Joint pain and muscular ache (lower back pain, joint pain, pain in a limb, general back ache)					
3	Excessive sweating (unexpected/sudden episodes of sweating, hot flushes independent of strain)					
4	Sleep problems (difficulty in falling asleep, difficulty in sleeping through, waking up early and feeling tired, poor sleep, sleeplessness)					
5	Increased need for sleep, often feeling tired					
6	Irritability (feeling aggressive, easily upset about little things, moody					
7	Nervousness (inner tension, restlessness)					
8	Anxiety (feeling panicky)					
9	Physical exhaustion/lacking vitality (general decrease in performance, reduced activity, feeling of getting less done, of having to force oneself to undertake activities)					
10	Decrease in muscular strength (feeling weak)					
11	Depressive mood (feeling down, sad, on the verge of tears, mood swings)					
12	Feeling that you have passed your peak					
13	Feeling burnt out, having hit rock-bottom					
14	Decrease in beard growth					
15	Decrease in the number of morning erections					
16	Decrease in ability/frequency to perform sexually					
17	Decrease in sexual desire/libido (lacking pleasure in sex, lacking desire for intercourse)					

The text is preceded by ''Which of the following symptoms apply to you at this time? Please mark the appropriate box for each symptom. For symptoms that do not apply, please mark 'none'. 1 = none, 2 = mild, 3 = moderate, 4 = severe, 5 = extremely severe. Thank you very much for your cooperation.''(33)

This screening tool is validated and it can reasonably measure quality of life , changes following treatment, and the wide range of symptoms and their severity seen in LOH. It has 17 items and it allows for a 5 point ordinal rating scale. It also allows to categorize patients as :

1) Little or no complaints (total score <26)

2) Mild complaints(score 27–36)

3) Moderate complaints (score 37–49)

4) Severe complaints (score >50).

Serial documentation of this screening tool will also be helpful in assessing progression of disease and treatment response. (32). It was not initially developed as a screening tool for diagnosis of hypogonadism . However studies later have shown that it has a sensitivity of 83–96% which suggests that it is good screening tool for diagnosis of late onset hypogonadism (34). Specificity of the AMS score was however only 39% and hence it needs to be followed up by a biochemical test to confirm the diagnosis of hypogonadism.

The other patient questionnaires used and validated in the USA are the ADAM and MMAS Questionnaires. These questionnaires also assess how ageing affects a person's sexuality, erectile function, physical strength, and feelings of well-being .

ADAM questionnaire

The ADAM questionnaire was developed in 2000.

***TABLE 5: ADAM QUESTIONNAIRE*(35)**

1	Do you have a decrease in libido (sex drive)?	Yes	No
2	Do you have a lack of energy?	Yes	No
3	Do you have a decrease in strength and/or endurance?	Yes	No
4	Have you lost height?	Yes	No
5	Have you noticed a decreased "enjoyment of life"	Yes	No
6	Are you sad and/or grumpy?	Yes	No
7	Are your erections less strong?	Yes	No
8	Have you noticed a recent deterioration in your ability to play sports?	Yes	No
9	Are you falling asleep after dinner?	Yes	No
10	Has there been a recent deterioration in your work performance?	Yes	No
If you Answer Yes to number 1 or 7 or if you answer Yes to more than 3 questions, you may have low Testosterone.			

ADAM questionnaire consists of 10 questions which are related to androgen deficiency which needs to be answered with ‘‘yes’’ or ‘‘no.’’ It was initially published by Morley et al. They showed a sensitivity of 88%(35). Various other studies have been done following this to validate this screening tool and it was found that it had a sensitivity as high as 97% also. Even though its sensitivity is high, its specificity is only 24–60%(36) , (37). It is hence considered a very good screening tool. However its use beyond screening is limited. A biochemical analysis needs to follow through after screening patients with this tool. In a prospective study, the association between the ADAM questionnaire and serum hormone values was evaluated , and it found that free testosterone and dehydroepiandrosterone sulphate (DHEA-S) are lower in men with a positive result on the ADAM questionnaire(3 out of 10 symptoms). (37).

There was however no relationship found between ADAM score and total testosterone values in any of these studies. It was also not a good tool for assessing the symptom improvement after treatment of the patients with hypogonadism. A modified ADAM scale, the q ADAM scale was proposed by Mohamed et al. Which makes each of the questions in ADAM scale more objective by asking the patient to rate each of their answers from 1-5 (1(terrible) 2(poor) 3(average) 4(good) 5(excellent)). (38) q ADAM has a better correlation with serum total testosterone level. It can also be used for assessing the symptoms over time.

The Massachusetts Male Aging Study questionnaire

The Massachusetts Male Aging Study questionnaire is another tool for screening . It was developed in 2000. It has 8 items in it and it is a self-administered questionnaire.

TABLE 6: MASSACHUSETTS MALE AGING STUDY QUESTIONNAIRE (39)

1	Age 60 or older	2 points
2	Receiving treatment for diabetes	3 points
3	Receiving treatment for asthma	1 point
4	Hours of sleep, less than 5 hours	1 point
5	Smoke cigarrettes, curretly or formerly	2 points
6	Bothered by headaches	2 points
7	Does not like directing other people's work	1 point
8	Height and weight boxes. 5'0" or under: ○ Under 135 lb ○ 135–150 lb ○ Over 150 lb 5'1"–5'3": ○ Under 150 lb ○ 150–165 lb ○ Over 165 lb 5'4"–5'6": ○ Under 160 lb ○ 160–180 lb ○ Over 180 lb 5'7"–5'9": ○ Under 180 lb ○ 180–195 lb ○ Over 195 lb 5'10"–6': ○ Under 195 lb ○ 195–215 lb ○ Over 215 lb 6'1"–6'3": ○ Under 210 lb ○ 210–235 lb ○ Over 235 lb 6'4"–6'6": ○ Under 230 lb ○ 230–255 lb ○ Over 255 lb 6'7" or over: ○ Under 245 lb ○ 245–275 lb ○ Over 275 lb Middle category Bottom category	 2 points 3 points

The sensitivity of MMAS 76% and its specificity is 49%. (39). Later studies have shown a sensitivity of 60 % also for MMAS questionnaire. (34). The advantage of this screening tool is that it is a self-administered screening questionnaire. However its sensitivity and specificity is poor. There aren't any studies that has looked into the independent association between serum testosterone values and MMAS questions individually, or total overall score.

The New England Research Institute (NERI) Hypogonadism Questionnaire

The New England Research Institute (NERI) Hypogonadism Questionnaire (40)was developed in 2009. It was developed specifically to screen for hypogonadism. It initially consisted of 67 items . It was later modified to contain 25 items. However, till date there is no study done to look into its sensitivity and specificity and hence it is not used in clinical practice yet.

A.M. Bernie et al. did a comparison of the different screening questionnaires for screening hypogonadism. The results of the same are summarised in the table below.

TABLE 7: COMPARISON OF QUESTIONNAIRES USED FOR SCREENING FOR HYPOGONADISM (41)

	Year of development	Number of questions	Sensitivity	Specificity	Advantages	Disadvantages
ADAM and qADAM	2000	10	83.3–97%	19.7–36.6%	High sensitivity makes it ideal for screening test	Not all studies have shown a direct correlation with the ADAM and decreased serum androgen levels
AMS Rating Scale	1999	17	83–96%	24–39%	Also has a high sensitivity, making it a reasonable choice as a screening questionnaire	Not developed as a screening tool for LOH. It's more of a quality-of-life scale for aging men and not related to testosterone levels
MMAS questionnaire	2000	8	59.9–76%	42.9–59%	Shortest of the screening questionnaires for LOH	Clinical data suggest that it is not the most accurate assessment tool
NERI Hypogonadism Questionnaire	2009	25	N/A	N/A	Has good test-retest reliability and internal consistency as well as validity	There has yet to be a study looking at the questionnaires' sensitivity, and thus its ability to act as a screening tool

Screening tools are useful as it takes very less time to be filled and many times it can be filled by the patient themselves. It can be filled when patients are in the waiting area to meet clinicians. Whether further exploration and evaluation of hypogonadism is needed or not can be decided based on screening tools. It is useful in places where patients are culturally inhibited to talk about symptoms of hypogonadism. In these cases, screening tools help bring out symptoms that otherwise would have been missed.

TESTOSTERONE CUT OFF FOR DIAGNOSIS OF HYPOGONADISM

The symptoms of late onset hypogonadism presents differently in different individuals. It is very subtle in some while very obvious in others. Therefore the diagnosis of hypogonadism cannot be made just based on clinical symptoms. Biochemical evaluation with serum total and free testosterone needs to be done in order to make a diagnosis of hypogonadism.

There is however no universally agreed definition for the cut-off point of testosterone at which a diagnosis of LOH can be made. This is mainly because the symptoms are varied even with same testosterone levels in different individuals.

(European Male Aging Study, EMAS, was one of the biggest studies conducted to recognise symptoms and signs of testosterone deficiency in elderly men. They found three main sexual symptoms (decreased morning erection and sexual thoughts and erectile dysfunction) were almost always associated with a late onset hypogonadism. They suggested that the presence of at least these three sexual symptoms with a total testosterone level of less than 11 nmol/L and free T < 225 pmol/L is needed to diagnose late onset hypogonadism.(42)

According to endocrine society guidelines, a total testosterone less than 300 ng/dl is considered deficient(6). The American Urological Association also considers 300 ng/dl as cut off for hypogonadism (7) . The ISSAM and the ISSM however uses the cut off value of TT <12 nmol/L or 350 ng/dl.

TABLE 8:SOCIETY GUIDELINES ON TOTAL AND FREE TESTOSTERONE CUT OFF FOR HYPOGONADISM

Expert opinion	Cut-off **Values Total T (TT) or free T**	**Year of Release**
Endocrine Society	TT < 300 ng/dl or free T < 5 ng/dl	2018
AUA	TT < 300 ng/dl	2018
ISSAM	TT < 350 ng/dl (12 nmol/L) or free T < 65 pg/ml	2015
ISSM	TT < 350 ng/dl (12 nmol/L)	2015
EUA	TT <11 nmol/L and free T < 225 pmol/L	2015

The best time for sampling blood for testosterone assay is in the morning between 07.00 and 11.00 h(43). At least 2 samples needs to be ideally taken to allow for hormonal variation in different individuals at different point of time(28). This diurnal variation is not very well seen in older men. In a study conducted by Crawford et al. Testosterone values remained mostly the same from 6am to 2 pm and even after that dropped by only 13 %. (44) The total testosterone levels, if low indicates low gonadal function.

The number of symptoms of hypogonadism increases as testosterone levels reduces. A study done by Zitzmann et al. showed that symptoms like loss of libido and vigour occurred with testosterone levels below 15 nmol/litre itself. Symptoms of depression and type 2 diabetes mellitus were higher in men with total testosterone levels below 10 nmol/litre. Erectile dysfunction due to low testosterone was found in men with testosterone concentrations below 8 nmol/litre. However erectile dysfunction could be due to multiple aetiologies including metabolic risk factors, smoking, and depression. (45)

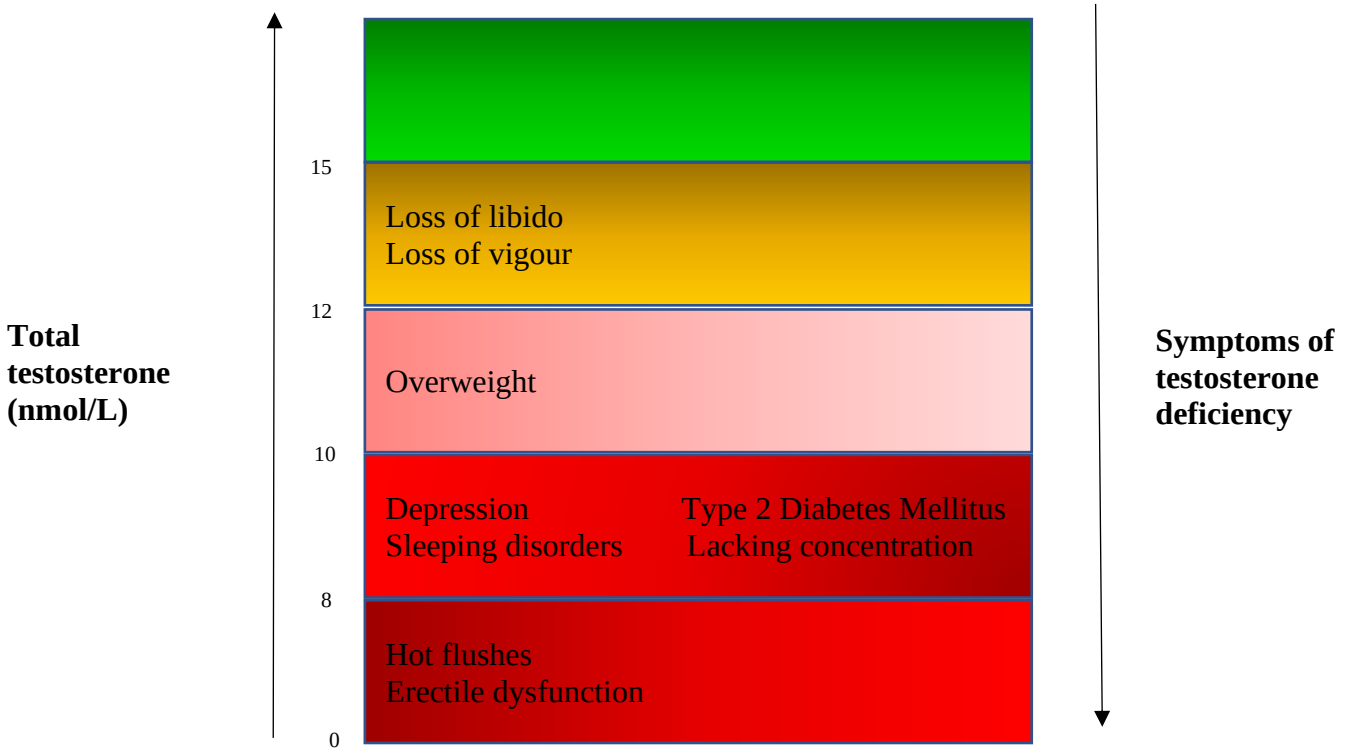


FIGURE 3: TESTOSTERONE LEVELS AND SYMPTOMS(45)

If the clinical picture does not correspond with the testosterone levels obtained, free or bioavailable Testosterone should be considered. This is because variations in SHBG concentrations can influence the total testosterone values. Free or bioavailable testosterone should especially be considered in obese men as they are known to have low levels of SHBG. The gold standard for measurement of free T is Equilibrium dialysis , but it may not be available routinely or may be very costly. Free Testosterone assays which are based on analog displacement immunoassays are available widely and they have been used with good success. However, its reliability is questionable. Another alternative is to measure serum SHBG and serum total testosterone in a reliable lab and to calculate the free testosterone using an equation. (46).

Measurement of LH will help in differentiating between primary and secondary hypogonadism . If LH is elevated and total testosterone is low, it indicates testicular failure. On the other hand, if LH is low in hypogonadal men , central causes of hypogonadism should be looked into (47).

The difference in symptoms between men with same level of testosterone or free testosterone in the body is also thought to be contributed by the level of sensitivity of androgen receptors in various individuals. The mechanism by which androgen receptors act is by direct regulation of gene transcription. AR gene has 8 exons. Exon one of this gene has a polymorphic sequence of CAG repeat. The number of CAG repeats is negatively associated with the transcriptional activity of androgen receptor. (48). This difference among individuals can cause difficulty in having a single cut off value for hypogonadism. It can also have implications on the dose of testosterone therapy and the effect of therapy in various individuals.

The parameters that need to be evaluated in a person with suspected hypogonadism include LH, TSH, SHBG, prolactin and vitamin D.

TREATMENT WITH TESTOSTERONE IN OLDER MEN WITH AGE-RELATED DECLINE IN TESTOSTERONE CONCENTRATION

Whether to treat age related decline in testosterone is still controversial. The endocrine society guidelines suggest against routine treatment of older men(65 years or older) with low testosterone in the serum. It is suggested that clinicians can offer therapy in men who are >65 years if there is significant symptoms or conditions that suggest testosterone deficiency and if they have consistently and unequivocally low morning testosterone . It should be on an individualised basis and the potentials risks and benefits of therapy should be extensively discussed with the patient before starting therapy. (6)

The European association of urology suggests treating adult men with low serum testosterone and consistent and if possible multiple symptoms and signs of hypogonadism following unsuccessful treatment of obesity and other comorbidities(30).

Prior to offering testosterone therapy, haemoglobin and haematocrit should be measured and it should be withheld if haematocrit exceeds 50%. Haemoglobin should also be measured at 3, 6 and12 months after starting testosterone replacement therapy. While on TRT, haematocrit over 54% requires intervention in the form of dose reduction or temporary discontinuation. Patients should be informed about the risk of polycythaemia prior to therapy with testosterone. In men aged 40 and above, PSA should also be measured prior to testosterone therapy. This is to prevent giving testosterone to patients with occult prostate cancer. (7)

The goal of testosterone replacement therapy is to achieve a total testosterone level in the middle tertile of the normal physiologic range which is 450–600 ng/dl(6). The treating physician and patient should discuss and decide on the choice of testosterone formulation. Short acting preparations are preferred for initial treatment as it will be easier to discontinue it in case of adverse effects. It is preferrable to prescribe Commercially manufactured testosterone rather than compounded testosterone, when possible. More frequent monitoring and dose adjustment is needed in case of prescribing compounded testosterone.

A list of all the dosing formulations of testosterone available are given in table 9

TABLE 9: DOSING FORMULATIONS OF TESTOSTERONE AVAILABLE(6)

Formulation	Typical Starting Doses	Pharmacokinetic Profile	Advantages	Disadvantages
T enanthate or cypionate	150–200 mg IM every 2 wk or 75–100 mg/wk	Serum testosterone rise into the supraphysiological range after a single injection, then decline slowly to hypogonadal range by the end of the dosing interval	Relatively less expensive and administered by self, dosing is flexible	IM injections are needed Peak value and low value of serum testosterone may be associated with fluctuation in symptoms
T transdermal gels: 1%, 1.62%, or 2%	50–100 mg of 1% transdermal gel; 20.25–81 mg of 1.62% gel or 40–70 mg of 2% transdermal gel applied to skin	Restore testosterone to normal physiological range, has less fluctuation	Dosing flexibility, can be applied easily, has good skin tolerability; less erythrocytosis	Potential of transfer to other members of the family, occasional skin irritation, high DHT concentrations(unknown significance), testosterone concentration may vary with each application
T Axillary Solution	60 mg of Testosterone	Restores testosterone to normal range	Good skin tolerability	Potential of transfer to other members of the family, occasional skin irritation, high

	solution applied in the axillae			DHT concentrations(unknown significance), testosterone concentration may vary with each application
Transdermal T patch	One or two patches, designed to nominally deliver 2–4 mg of T for 24 h, to be applied daily on non-pressure areas	Restores serum T, DHT, and E2 concentrations to the physiological male range	Can be easily applied	Skin irritation is possible; patients with very low testosterone may need two patches per day
Buccal, bio-adhesive T tablets	30-mg controlled release, bio-adhesive tablets twice daily	Restores serum T, DHT, and E2 concentrations to the physiological male range; absorption from the buccal mucosa	Convenient and discreet	Adverse effects related to gum
T pellets	Pellets containing 600–1200 mg T implanted SC	Serum T peaks at 1 month and then is sustained in normal range for 3–6 months, depending on formulation	Less frequent administration	Requires surgical incision foreach insertions; pellets may get extruded spontaneously; local reaction, hematoma and infection may occur rarely
Injectable long-acting T undecanoate in oil	750 mg IM, followed by 750 mg at 4 wk., and 750 mg every 10 wk.	When administered at a dose of 750 mg IM, serum T concentrations are maintained in the normal range in most treated men	Less frequent administration	Requires IM injection ; coughing in a small number of men immediately after administration;
Nasal T gel	11 mg two or three times daily	Serum T concentrations are maintained in the normal range in most treated men	Rapid absorption; first pass metabolism avoided	Multiple daily intranasal dosing needed; local side effects in the nose, not appropriate for those with nasal disorders

EFFICACY

Few studies are only present looking at the efficacy of testosterone therapy.

Sexual function: Studies suggest that testosterone therapy is associated with Significant improvements in sexual desire , spontaneous erections and sexual motivation(49). However it does not improve ejaculatory function(50).

Well-being and depressive symptoms: Testosterone therapy improves mood. It improves the positive parameters of mood and reduces the negative parameters of mood(51). However the

changes in mood are seen in the early replacement periods and further increase in testosterone did not result in improvement in mood.

Bone mineral density : Testosterone therapy improves the bone mineral density, bone strength. The effect is more in the trabecular than peripheral bone and more in the spine than hip. However there are no studies on the effect testosterone has on fracture risk (52). However testosterone monotherapy is not recommended for men with osteoporosis.

Body composition, muscle strength, and physical function: Testosterone therapy in men with hypogonadism increases lean body mass and muscle strength . Testosterone administration reduces fat in the body as well. However, studies have not shown improvements in gait speed or measures of disability consistently(53)

Cognitive function: Studies done till date has not shown any major improvement in cognitive function with testosterone therapy(54)

ADVERSE REACTIONS

Testosterone therapy has some side effects. Most common drug-related adverse events are oiliness of skin , acne and breast tenderness. Some conditions are associated with high risk of adverse events and it is preferable to not give it in these men. Other side effects include:

- Erythrocytosis : testosterone therapy is associated with a dose and testosterone concentration related increase in haematocrit(> 54%). Therapy with testosterone should be withheld if haematocrit increases. (87)

- Cardiovascular : there are no large RCTs or meta-analysis to conclusively say whether testosterone therapy will cause significant cardiovascular risks. Some studies suggest that cardiovascular risk is higher If testosterone concentration in the body is low. (90)
- Venous thromboembolism: Few case control studies and epidemiological studies have shown a mild increase in venous thromboembolism. However the results are inconclusive. There are no RCTs or meta-analysis on the same.
- Prostate: The relationship between prostate cancer and testosterone therapy is also not very well understood. Meta analysis on epidemiological studies have not shown any significant association between development of prostate cancer and testosterone therapy. Prostate and breast cancers are hormone dependent cancers. Hence it's not advisable to give testosterone in patients with either of these diseases. Prostate evaluation and PSA needs to be done prior to testosterone therapy. Patients with high PSA should not be given testosterone therapy. Some men have small cluster of prostate cancer cells that is not clinically evident. Whether testosterone therapy causes these to progress to overt cancer is not known yet.
- Lower urinary tract symptoms.: Testosterone therapy does not worsen LUTs in men who did not have severe LUTs to begin with.124 Whether it will worsen LUTs significantly in those who has severe LUTs at baseline is not well studied.
- Fertility : Therapy with testosterone suppresses spermatogenesis and is not ideal in treatment of men who desire fertility in the next 6-12 months. This is especially not indicated if they have hypogonadotropic hypogonadism
- Miscellaneous: It can cause retention of fluid and oedema and can theoretically worsen heart failure.

Few conditions are associated with very high risk of serious outcomes with testosterone therapy.

Very high risk of serious adverse outcomes: Metastatic prostate cancer and breast cancer are associated with increased risk.

Moderate to high risk of adverse outcomes: Testosterone therapy in men with unevaluated prostate nodule or induration, unevaluated PSA > 4 ng/ml , haematocrit >48% , severe LUTS associated with benign prostatic hypertrophy, uncontrolled or poorly controlled congestive heart failure are associated with high risk of adverse outcomes. It is hence not recommended to give testosterone on these patients. (6)

HYPOGONADISM AND TYPE 2 DIABETES MELLITUS

The prevalence of diabetes mellitus is increasing day by day. With increasing life expectancy , the number of patients with diabetes mellitus is increasing even more. It causes increased morbidity and mortality due to its microvascular and macrovascular complications.

Insulin resistance is an important feature of Type 2 Diabetes Mellitus . Many recent studies are suggesting a relation between insulin sensitivity and testosterone levels in the body . There seems to be an inverse relationship between testosterone and insulin resistance (55),(56). Few studies suggests that low testosterone levels may predict insulin resistance and the future development of type 2 diabetes. (57). Studies also show low testosterone levels in diabetic men when compared with nondiabetic men. (58). There seems to be a bidirectional relationship between testosterone levels an diabetes mellitus . However, the effect poorly controlled diabetes mellitus has on testosterone levels seems to be higher than the effect low testosterone levels have on promoting diabetes. (59)

Twenty-one percent of diabetic men compared with 13% of nondiabetic men had hypogonadism according to a study in a southern California population. In a study conducted in Asian Indian men ,

15 % of men who had diabetes were found to have hypogonadism . 73 % of them had hypogonadotropic hypogonadism and the rest 27 % had hypergonadotropic hypogonadism. The prevalence of hypogonadism in the control group was only 10 %. (60) . In another study, 43 % of all men (n - 249) with type 2 diabetes mellitus had low TT levels (<10 nmol/litre)(61). A study done by Agarwal et al. in 10 centres in India found 20.7% prevalence of hypogonadism in men with type 2 Diabetes Mellitus(62)

Various mechanisms play a role in causing hypogonadism in patients with diabetes mellitus. In diabetic men , the SHBG levels are low. This does not however mean that the free testosterone levels are high . Diabetes have a low total testosterone and a low free testosterone even though they have low SHBG(63). In spite of the low testosterone in these patients , there is no increase in gonadotropins noticed (58). So , there is a central gonadal axis suppression also that contributes to hypogonadism in diabetics. This mainly occurs at the hypothalamus level . Impaired insulin signalling in the CNS cause hypothalamic suppression, at least in part via effects on KNDY (kisspeptin/neurokinin B/dynorphin) neurons in the arcuate nucleus of the hypothalamus(58), (64). Hypothalamic inflammation is proposed to cause hypogonadism in diabetics . In a recent experimental study in adult men, it was found that infusing the pro-inflammatory cytokine interleukin- 2 (IL-2) at a relatively low dose reduced LH stimulated testosterone secretion and augmented testosterone-mediated negative LH feedback(65). A role for genetic susceptibly, and auto-immunity are also proposed as mechanism of hypogonadism in diabetics , however there isn't as much evidence for the same . Insulin also has a direct role in promoting GNRH secretion in a hypothalamic GNRH neuronal cell line , gonadotropin secretion from pituitary cell cultures , and testosterone secretion from cultured Leydig cells. Low testosterone causes an alteration in Leydig cell function, the molecular mechanism for which is still unknown (66).

Studies also provide evidence on mechanisms by which low testosterone causes diabetes mellitus . Testosterone reduces pro-inflammatory cytokines in vitro and in vivo, causing increase in insulin sensitivity in both muscle and adipose tissue(61). Androgenic signalling augments glucose-stimulated insulin secretion in beta cells via amplifying the incretin effect of glucagon-like peptide1 . Aromatization of testosterone to oestradiol is also required to improve glucose metabolism . Hence low level of testosterone or aromatase enzyme, that causes low oestradiol is also one of the mechanisms leading to diabetes mellitus. Among men with late onset hypogonadism , only those with testosterone of <8 nmol/L had an increased prevalence of insulin resistance (67).

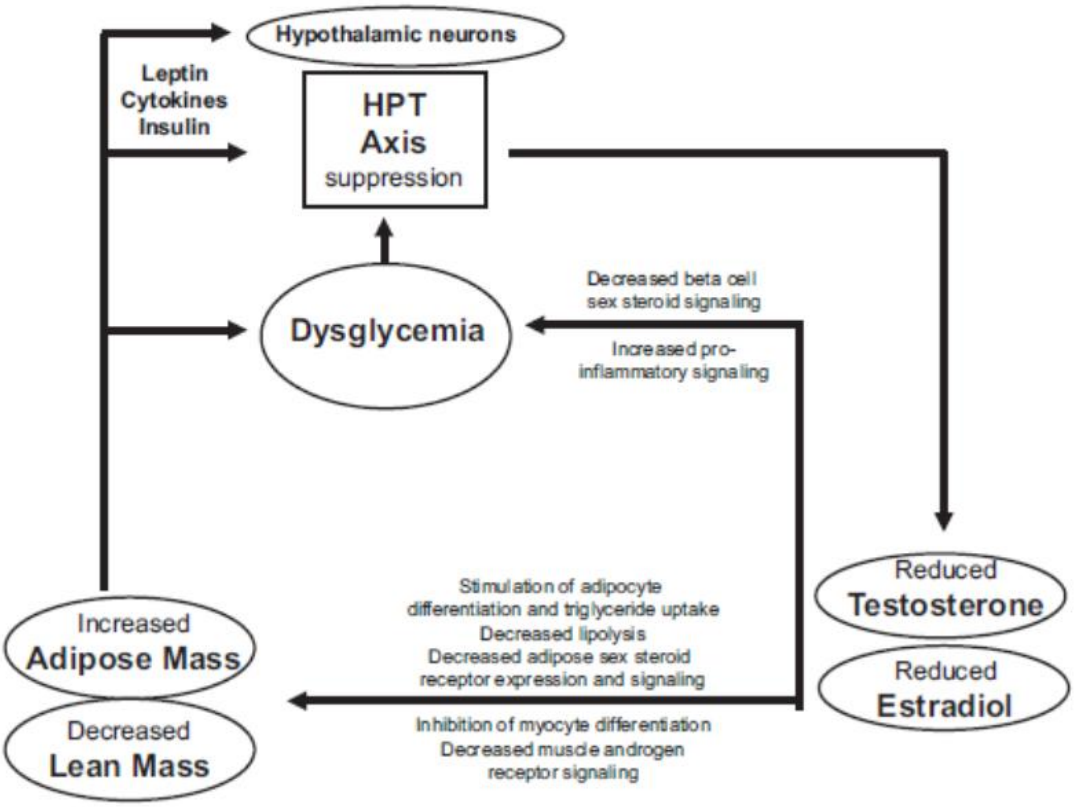


FIGURE 4: THE BIDIRECTIONAL RELATIONSHIP BETWEEN TESTOSTERONE AND DIABETES MELLITUS(68).

In most but not all studies testosterone treatment improves insulin resistance to a modest degree, but effects on glycaemic control remain inconsistent(61). Current recommendations therefore does not recommend testosterone testing or replacement therapy as a routine in patients with diabetes mellitus.

HYPOGONADISM AND HYPERTENSION

Hypertension is another major adverse health factor in the aging population. Some studies also show an association of hypertension and hypogonadism. However, there are only very few studies pertaining to the same.

One study done showed that , in those with hypertension, the prevalence rate of hypogonadism was 42.4%. The same study also showed that in patients with hypertension, the relative risk of hypogonadism was 1.84(69) The European male ageing study also showed that men with a history of hypertension have a higher crude prevalence of hypogonadism than men without a history of hypertension. Among hypogonadal men with hypertension, there was also a statistically significant decrease in ability/frequency to perform sexually . Men with history of arterial hypertension had 3.68-fold higher odds of developing hypogonadism compared to men without hypogonadism. Regardless of other comorbidities and men's age, hypertension decreased the level of both total and free testosterone by 0.47 and 2.52 units, respectively. In this study, they however noticed that among patients with hypogonadism, systolic blood pressure was statistically significantly increased, but diastolic did not change(70). In Massachusetts Male Aging study done in the USA, it was demonstrated that in patients with hypogonadism, both systolic and diastolic blood pressure was higher than in patients with a normal testosterone level(71). So, the relationship between hypertension and hypogonadism seem to be bidirectional. Further studies are however needed on the relationship between hypogonadism and hypertension . The pathophysiology of the same is also yet to be studied. Whether, routine testosterone testing and treatment for hypogonadism will be beneficial or not in men presenting with hypertension need to be studied further.

HYPOGONADISM AND CARDIOVASCULAR DISEASE

Cardiovascular disease (CVD) is the world's leading killer disease(72). Men seems to have a greater mortality risk due to cardiovascular disease when compared to women . It was hence initially

thought that oestrogen is protective while testosterone increases the risk for cardiovascular disease. However, cross sectional studies and meta- analysis suggest that, low testosterone can increase the risk of cardiovascular mortality (73), (74). The European Prospective Investigation into cancer Norfolk study found that everyone standard deviation increase in baseline testosterone was associated with a 14% risk reduction in mortality over 6-10 years due to cardiovascular mortality.

A meta-analysis done showed that the association between testosterone and cardiovascular mortality is significant in elderly men while it is not so significant in middle aged men. 11 prospective studies showed a statistically significant inverse association between endogenous testosterone and cardiovascular disease/mortality in elderly men. Different viewpoints are postulated for this difference seen. Low testosterone might have a distinctly different effect between middle-aged and elderly men with respect to the adaptive response of adipose tissue which might in turn cause obesity in elderly which might result in high CVD risk.(75)

Different pathophysiology are described for the cause of the association between hypogonadism and cardiovascular disease. They are :

Increase risk of other risk factors of cardiovascular disease: Low testosterone is associated with an increased risk and prevalence of dyslipidaemia, obesity, hypertension and diabetes mellitus which are all well known risk factors of cardiovascular disease(76).

Inflammation - Inflammation is a key component of atherosclerosis as it has a role in the early development of the atherosclerotic plaque. Various small studies suggest that testosterone has a role in immune modulation and in decreasing the inflammatory component in atherosclerosis (77). Various studies have shown that testosterone replacement in men decreases the levels of

endogenous inflammatory cytokines like TNF-α, IL-6, and IL-β which are implicated in atherosclerosis(78). C-reactive protein (CRP) ,which is a marker of general inflammation is also used as a marker of atherosclerotic cardiovascular disease. An inverse correlation have been found between CRP and testosterone levels (79). Studies does not however show any correlation between testosterone therapy and CRP. Conclusive evidence on the association of inflammation and hypogonadism is still lacking.

Atherosclerosis Mediating Molecules*:* Vascular Cell Adhesion Molecule (VCAM) is one of the molecules that is a major contributor to the formation of the fatty streak, the initial lesion in atherosclerosis as it permits the migration of macrophages into the vascular wall. VCAM levels inversely correlated with testosterone levels in a study on patients with cardiovascular disease(80). However, testosterone replacement in hypogonadal men was not shown to affect serum levels of VCAM . Further research with higher dose and longer duration of treatment are however needed

Endothelial Function and Vascular Health :Endothelial dysfunction is one important risk factor for cardiovascular disease. Cross-sectional studies showed that low testosterone level was associated with endothelial dysfunction (81). Prospective studies on testosterone-treated men with CAD suggested that testosterone was able to improve their endothelial function . Yet, the effect of testosterone replacement of hypogonadal men on endothelial function has yielded controversial results, which varied by the dosage form of testosterone. Other studies assessed the effect of testosterone levels on arterial stiffness, which is also an important risk factor of coronary artery disease . Epidemiological studies showed an inverse correlation between testosterone levels with arterial stiffness (82), and testosterone. Replacement decreased arterial stiffness .

Myocardial Health: It has been suggested that testosterone probably has direct effects on ventricular repolarization of the myocardium . Evidence suggests that testosterone protects from myocardial

ischemia. Small randomized trials have shown improved exercise capacity and increased time to ST depression as well as decreased frequency of anginal attacks with testosterone therapy (83).Testosterone therapy also has been shown to increase cardiac output in patients with heart failure (84).

Though evidence on the association of cardiovascular disease and hypogonadism is becoming increasingly apparent, whether testosterone replacement therapy will be beneficial in those with hypogonadism is yet to be well studied. The two main concerns of testosterone therapy is that, it might promote coronary heart disease and acute coronary syndromes and that it might promote prostate cancer (85). Other adverse effects include increase in haemoglobin and haematocrit, and a small decrease in HDL cholesterol. Evidence is still limited on it and the ideal dose is yet to be determined (76).

HYPOGONADISM AND FRAILTY

Frailty is a physical condition in which people are in a vulnerable health status and is in high chance of developing overt disability.(86)Frailty increases adverse outcomes such as disability, hospitalisation and mortality. The definition of frailty as per the FRIED Frailty tool is as in Table 10

TABLE 10: FRIED FRAILTY TOOL

Weight loss (≥5 percent of body weight in last year)
Exhaustion (using the CES – D depression scale)
Weakness (decreased grip strength)
Slow walking speed (gait speed) (>6 to 7 seconds to walk 15 feet)
Decreased physical activity (kcals spent per week: males expending <383 kcals and females <270 kcal)
FRAIL: Three or more out of the five criteria PRE-FRAIL: One or two out of the five criteria

Frailty phenotype(FRIED Frailty Tool)(86)

Multiple inter- related dysregulation across many physiological systems play a role in frailty. It's a declining cycle of events with one factor leading to the other. Initially, there is a decline in energy and reserve, which leads to decline in muscle mass and strength which in turn lead to poorer walking speed and energy levels, which results in reduced levels of physical activity, and finally it again serve to further accelerate physical decline. This mutually exacerbating declining cycle is called frailty cycle.

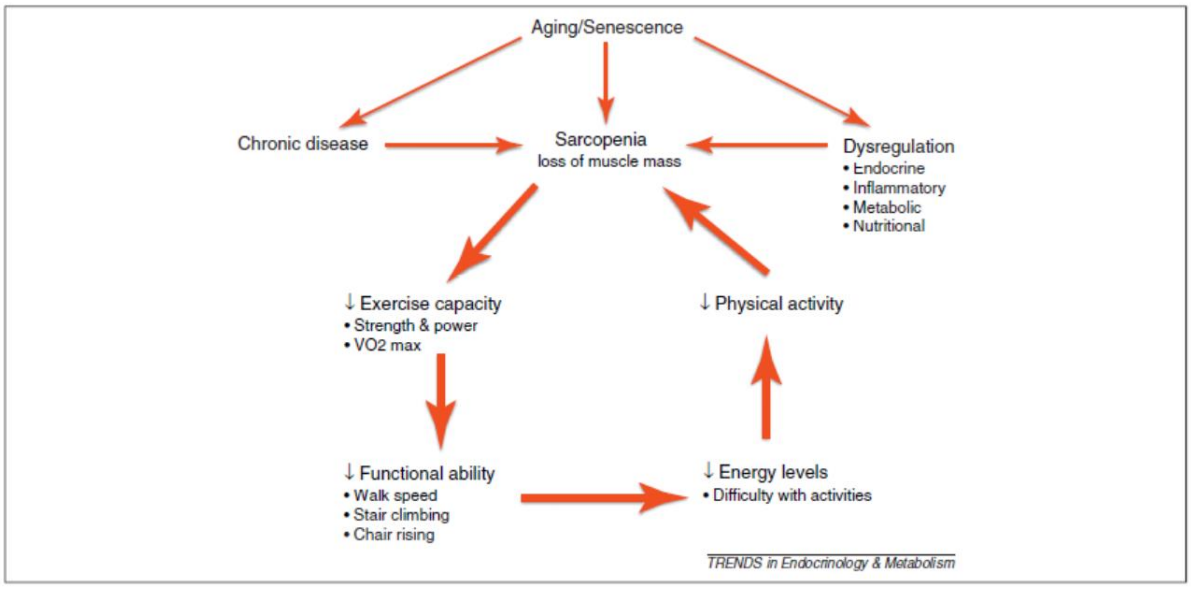


FIGURE 5: FRAILTY CYCLE(87)

The core feature of frailty is loss of muscle mass. As age advances, all human beings experience a significant loss of muscle mass and strength that in turn increases the risk of falls, fractures and disability. Decline in function and increased dependence in older individuals place a large burden on healthcare services and also incur incalculable losses in the quality of life of the person involved and his/her family. Studies show that frailty in older men is associated with poorer health and increased risk of mortality(88). Muscle strength and muscle mass is closely related to anabolic steroids in the body. Testosterone, being an anabolic steroid has been extensively studies in relation to frailty.

In one large study in the Netherlands, low levels of sex hormones were associated with impaired mobility and low muscle strength in men, but there was no significant correlation in women(89). Studies also show an association between reduced physical performance and low testosterone levels in men. Falls are common in older individuals. Risk of fall was higher in men with lower bioavailable testosterone levels(free testosterone). This association of testosterone level and fall was independent of lower physical performance. This suggests that the effect of testosterone on risk of fall may be mediated by other actions of the androgen also (90). One study showed that free testosterone, but not total testosterone was directly related to arm and leg strength(91). In Massachusetts male ageing study, a significant correlation was observed between SHBG and frailty(92)

While the correlation between muscle strength and testosterone levels seem to be modest, the association between muscle mass and testosterone levels seems to be even more stronger(86). Sarcopenia or the reduction of muscle mass and/or function is an important component of frailty. It occurs due to a reduction in synthesis of protein along with an increase in muscle protein degradation as you age. There is a preferential loss of type II skeletal muscle fibres in age related loss of muscle mass(93). Testosterone therapy is theoretically thought to have a therapeutic effect on frailty and ageing. Lots of studies are underway to find out about the same. Androgens promote differentiation of mesenchymal multipotent cells into the myogenic lineage thereby increasing the muscle mass and also inhibit their differentiation to adipocytes. Studies have also shown that the skeletal muscle of geriatric men are as responsive to the effects of testosterone as those if young men(94). Thus age does not limit the beneficial effects of testosterone.

Though many studies show an association of frailty and testosterone levels, the relationship between the two is modest and not very consistent. Frailty is not due to a decline in a single system.

Multiple factors play a role in it. The decline in testosterone with ageing is also not very consistent. Low testosterone , hence cannot be considered as a cause of frailty, but it is very possibly one of the risk factors for frailty. This is consistent with the understanding that testosterone is not the only anabolic hormone in the body. Also, frailty is a multisystem abnormality and other factors like inflammatory, metabolic, cardiovascular and

nutritional dysregulation play a role in its pathophysiology, in addition to endocrinological dysregulation.

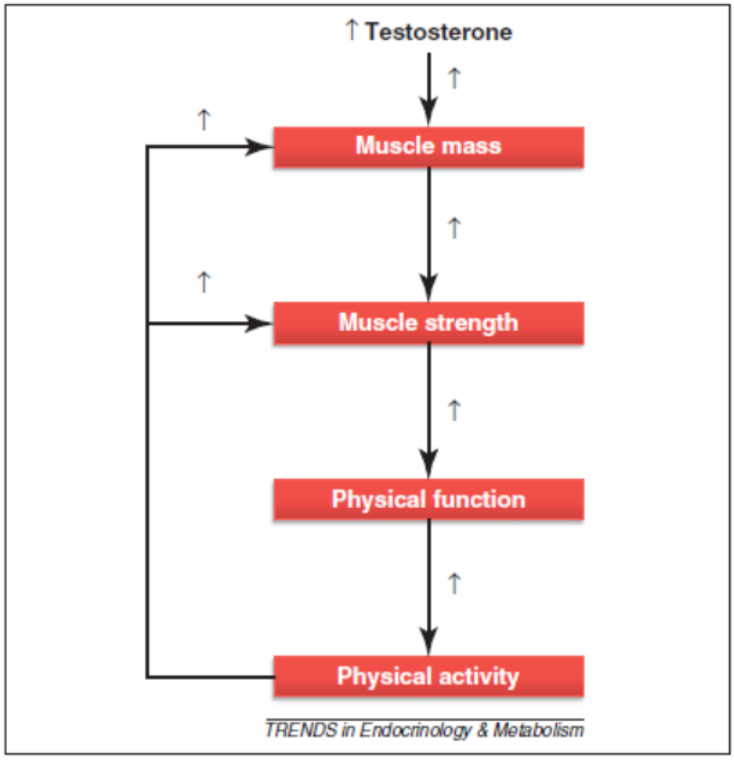


FIGURE 6: HYPOTHETICAL MECHANISM BY WHICH TESTOSTERONE CAN IMPROVE FRAILTY(87).

Figure 6 shows the hypothetical mechanism by which testosterone treatment can improve frailty. As testosterone levels increases, muscle mass and strength increases which leads to increased physical function and activity which in turn has a positive impact on muscle mass and strength .

Many studies are being done to look at the use of testosterone treatment in frail men. In a meta-analysis of testosterone or dihydrotestosterone replacement therapy in healthy men aged 65 and

older, 11 randomised trials were reviewed and it revealed that androgen therapy produced a moderate increase in muscle strength in men . There seems to be a larger effect on the lower limb muscle strength when compared to upper limb muscle strength in a subgroup analysis done in the same meta-analysis (95). In a randomised double blind study done by Shankar et al. Testosterone therapy for 6 months may prevent age-associated loss of lower limb muscle strength and improve body composition, quality of life, and physical function in intermediate-frail and frail elderly men with low to borderline-low testosterone. In another randomised double blind study done by Kenny et al, older, frail men when given testosterone replacement had increased testosterone levels and had favourable changes in body composition and modest changes in axial bone mineral density. However there was no substantial changes in physical function. A randomised study done by Travison et al. also showed that while there was improvement in muscle strength with testosterone therapy, the improvement in physical performance were not as apparent (96). Leg press strength, chest press strength, chest press power, total lean body mass (LM) and appendicular lean soft tissue mass(ASLT) showed a clear association with testosterone therapy , but grip strength, stair climb and gait speed were not as clearly associated. This might be due the fact that physical function is not just strength dependent . Better results might be obtained if therapy is combined with strength training.

Whether the results obtained during therapy will sustain once the therapy is stopped is also not known . Safety concerns are another major limitation for the use of testosterone therapy. The main concerns are related to cardiovascular mortality and prostate malignancy. It also causes erythrocytosis and increase in haematocrit. Currently, testosterone therapy is not advised fort treatment of frailty as its efficacy and safety profile is still not clear. Further larger and longer studies on frail men are warranted to extend the results of the studies already done.

HYPOGONADISM AND OSTEOPOROSIS

Although osteoporosis is predominantly an illness of the postmenopausal females, male osteoporosis and osteopenia and its consequences are significant. Men tend to attain osteoporotic fractures at least 10 years later in life when compared to women. However the morbidity and mortality associated with male osteoporotic fractures are quite significant and it might even be more than that in females. The prevalence of osteoporosis is very low in males below the age of 70 years. However, above 90 years of age, the prevalence is about 22.6 %(97).

Androgens have a close association with bone health. Bone growth and maintenance are affected by the level of testosterone in the body. Androgens helps in formation of bone in young men and in preventing bone loss in elderly men .

The skeletal system integrity in human beings is maintained by an intricate process named remodelling which is governed by the interplay of 3 major bone cells:

Bone-forming osteoblasts

Bone-resorbing osteoclasts

Mechanosensor/mediator osteocytes.

These cells are sensitive to sex hormones and any dysregulation in the function of these cells affect the bone health. In case of osteoporosis, there is increased bone resorption when compared to bone formation. Testosterone has different effect on these cells.

<u>Osteoblasts</u>

Osteoblasts are bone cells that are specialised for bone formation and has essential role in production of bone matrix proteins and bone mineralization. Androgen receptors are present on osteoblasts. Androgen receptors are upregulated in the presence of androgens(98). Studies shows

that both testosterone and 5α-dihydrotestosterone stimulates proliferation of cultured osteoblast precursors in distinctive species(99). Androgens are also found to have a role in reducing the apoptosis of osteoblasts(100). In essence, evidence suggests that androgens seems to have a positive impact on osteoblasts and thereby on bone formation(101).

Osteoclasts

Osteoclasts are mainly involved in bone resorption. It originates from the colony-forming unit-granulocyte macrophage hematopoietic cell lineage inside the bone marrow. Immature osteoblast release receptor activator of nuclear factor k-B ligand(RANK ligand) which binds to RANK on osteoclasts. This stimulates differentiation of osteoclast precursor cells(102). Osteoblast precursor also secretes osteoprotegin which also regulates the effect of RANKL on osteoclasts(103). Studies shows that osteoclasts proliferate after orchidectomy and is thought to be due to androgen deficiency. The effect of androgens on osteoclasts is indirectly through osteoblast precursors. Androgen deficiency cause increase in osteoblast precursors which secrete RANKL that causes increase in osteoclasts(104). Androgens also cause decrease in osteoprotegerin levels and thereby reduces the osteoclast formation . In effect, androgen deficiency causes increase in osteoclastic activity(103).

Osteocytes

During bone formation, a section of osteoblasts undergoes terminal separation and entombment by mineralized osteoid and they subsequently transforms to osteocytes. Osteocytes are encased in liquid-filled holes (lacunae) inside the mineralized bone and are found in plenty. It represents 90%–95% of the total bone cells. It possess long dendrite-like processes that interact with other osteocytes inside the mineralized bone and interact with osteoblasts on the bone surface. Osteocytes play an integral role in bone remodelling by responding to mechanical stimuli to prevent accumulation of bone microdamage.(105), (106). Studies shows that oestradiol prevent osteocyte

apoptosis and enhance the production of transforming growth factor-alpha which inhibits osteoclastic bone resorption(107). Though testosterone does not have a direct role on osteocytes, the oestrogens synthesised from testosterone in males may have a role.

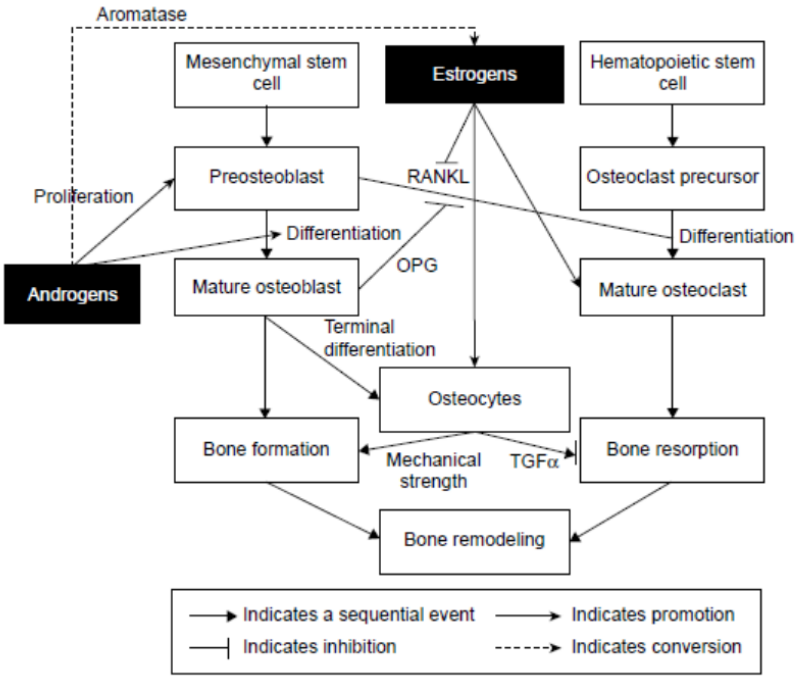


FIGURE 7: THE EFFECT OF ANDROGENS ON BONE CELL(106).

Bone health can be measured with fracture risk and bone mineral density. Studies have shown an association between bone mineral density and testosterone. In a case control study, hypogonadism was present in 58 % of subjects who had an osteoporotic fracture when compared to 18 % in controls(108). In a cross sectional study conducted in 6 centres in US, 2447 participants were included and the prevalence of osteoporosis in men with deficient testosterone was 12.3 % and it was 6 % in those with normal testosterone. Conversely , among men with osteoporosis , prevalence of testosterone deficiency was 6.9 5 compared to 3.2 % among men with normal bone mineral density. Thus there seems to be a bidirectional relationship between osteoporosis and hypogonadism(109). A meta-analysis done on 5 case control studies however showed no significant relation between osteoporosis and testosterone(110). One of the largest is the osteoporotic fractures in men study (MROS), followed thousands of men over the age of 65 in Sweden, the United States, and Hong Kong for an average of 4.5 years. Initial results of the study indicated that free

testosterone levels had a positive correlation with bone mineral density in the hip, femur, and arm but not the lumbar spine. Lower levels of free testosterone were also associated with increased risk of fracture. However, on doing further analysis of data using multivariate analysis in the same cohort, it was found that only bioavailable oestrogen (bioe2) and SHBG, not testosterone were independently associated with fracture risk(111).

There is hence conflicting evidence on the relationship between testosterone and bone mineral density . However studies have shown an association between E2 and bone mineral density . High E2 was associated with high bone mineral density . In men, 85 % of the serum E2 is derived by conversion of testosterone to E2 by aromatase. Therefore , low testosterone can potentially cause a low bone mineral density.

The association between testosterone and bone fracture has also been studied. Testosterone deficiency is associated with increased fracture risk according to some studies(109),(111). Some studies however does not show any association (112) . The effect of testosterone on fracture risk may however be not associated with just its effect on osteoporosis. Testosterone has an effect on muscle mass, muscle strength and physical activity which also contributes to reduction in falls and fracture risk.

Overall, low bioe2 and high SHBG, which correlates with a low bioavailable testosterone, contributes to low bone mineral density in men. Increased fracture risk is associated with low bioe2, low free testosterone, and high SHBG .

Testosterone therapy for the treatment of osteoporosis is being studied. Studies have mainly looked at the beneficial effects of testosterone therapy on bone mineral density. Testosterone therapy has

positive effects on bone mineral density. Hoppéa et al. Looked at 14 randomised trials and it concluded that testosterone therapy had a benefit in increasing at least the lumbar spine bone mineral density(113). Permpongkosol et al. , in an observational study showed significant bone mineral density increase with testosterone therapy. This study also showed that lumbar spine had a significant change noticed before femoral neck showed an increase in bone mineral density(114). An RCT done by Wang et al also showed a similar benefit of testosterone therapy on bone mineral density(115). However, the effect of testosterone therapy on fracture risk is not well studied(116). The endocrine society recommends testosterone treatment to enhance BMD only if they have truly symptomatic hypogonadism even though the ability of testosterone to improve BMD in hypogonadal males is known (116). This is due to the potential risks associated with testosterone therapy.

HYPOGONADISM AND OBESITY

Obesity, which is defined as a BMI more than 30 kg/m2 is a major issue in the world now. The global burden of obesity is increasing day by day. The revolutions in food industry, modern fast foods and the increasingly sedentary quality of work are all factors that contributed to the rising number of obese individuals in the world. According to world health organisation, in 2016, 39% of adults aged 18 years and over were overweight , and 13% were obese. (117). Obesity is an independent risk factor for several medical conditions and increases morbidity and mortality.
A bidirectional relationship between obesity and hypogonadism exists. Obesity is one of the biggest risk factor for development of hypogonadism.

Studies shows that as BMI increases the prevalence of hypogonadism also increases. Studies show a prevalence range of hypogonadism ranging between 45 % and 57.5 % in those with obesity(118), (119),(120)

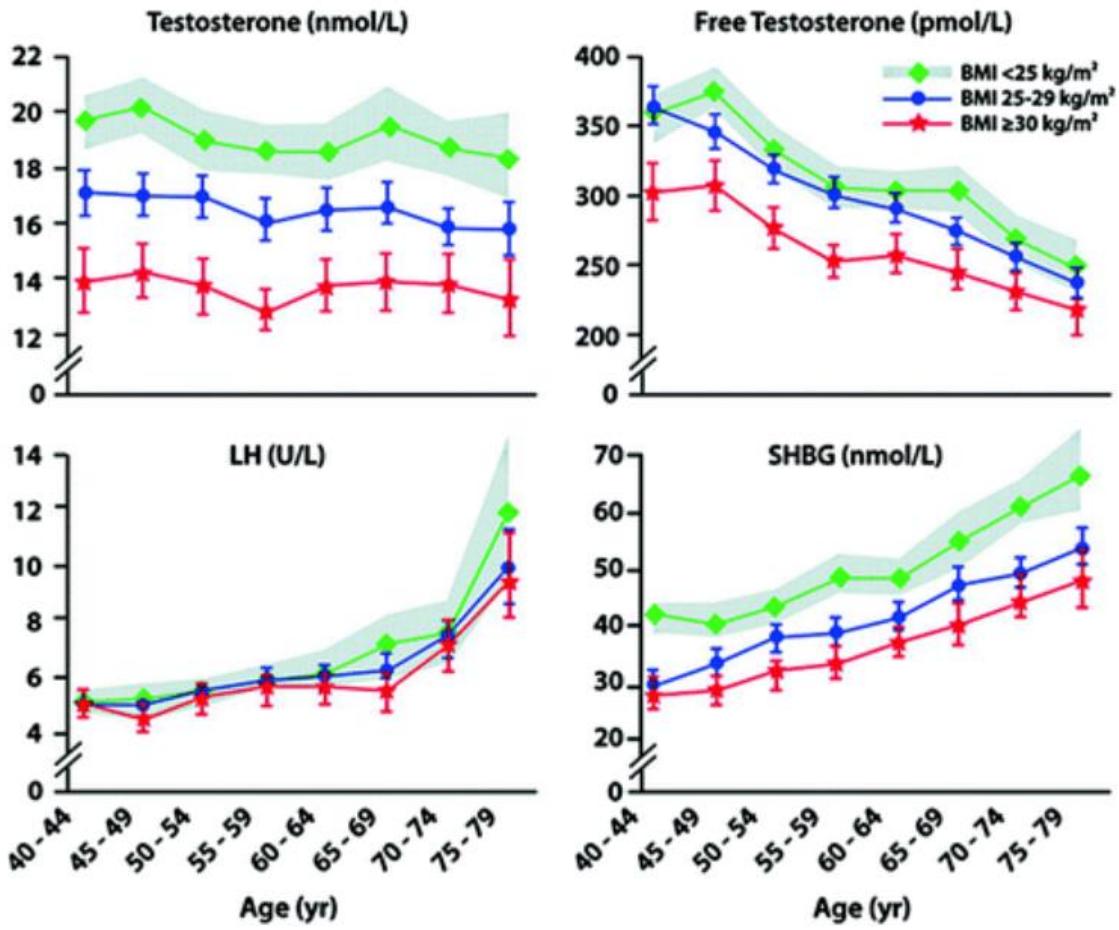


FIGURE 8: RELATIONSHIP BETWEEN AGE, BODY MASS INDEX AND HORMONES(121).

Obese men had a low testosterone value independent of their age. In obese men, the mean testosterone and the mean free testosterone levels were at least about 5 nmol/L and 55 pmol/L lower, respectively when compared to non-obese men of the same age (121). At least, 15 year age stratified difference was found between obese and non-obese men.

Testosterone deficiency increases obesity also. Rapid weight gain is observed in men following androgen deprivation therapy or surgical castration. This itself shows that testosterone deficiency causes increase in adipogenesis and visceral obesity(122). Testosterone deficiency is associated with visceral fat dysfunction which subsequently causes chronic inflammation, insulin resistance and low sex hormone binding globulin (SHBG) levels (123).

The exact mechanism for the interaction between hypogonadism and obesity is still being studies. Multiple studies are still underway to find the mechanism of this interaction. Various mechanisms have been proposed so far:

Hypogonadal–obesity hypothesis

Individuals with obesity and hypogonadism had a normal luteinising hormone (LH) and Follicle stimulating hormone (FSH) response when exposed to gonadotropin releasing Hormone (GNRH). This suggested that the pituitary was normal and that there might be a hypothalamic defect in these individuals(124).

Hypogonadal–obesity–adipocytokine hypothesis:

Hypogonadism and obesity have a vicious cycle. Cohens theory explains why body cannot produce compensatory testosterone even after production of increased gonadotrophins which stimulate Leydig cells. In obese individuals, the adipose tissue produce large amount of aromatase enzyme which causes conversion of testosterone to oestradiol and in effect reduce the testosterone levels in the body. The effectant testosterone deficiency further facilitates adipocyte differentiation, adipocyte inflammation and insulin resistance. This results in an increase in oestrogen, leptin, insulin and inflammatory cytokines which in effect causes hypothalamo–pituitary–testicular (HPT) axis suppression.

Testosterone-oestradiol shunt:

Obesity increases the expression of aromatase enzyme (CYP19A1) in the adipocytes. This enhances the conversion of androstenedione and testosterone to oestrone (E1) and oestradiol (E2) respectively in the body. The effective low testosterone in the body causes further increase in adipocytes which

again causes testosterone deficiency. The increased oestrogen in the body can also cause a negative feedback in the hypothalamo – pituitary level which can also cause further reduce testosterone.

Adipocyte hypertrophy and dysfunction

Adipocyte surface has lipoprotein lipase enzyme in abundance which hydrolyses circulating triglyceride-rich lipoproteins to free fatty acids. These free fatty acids are taken up by adipocytes and then esterified back to triglycerides which is then stored. Testosterone reduces the lipoprotein lipase activity in adipose tissue and therefore reduces triglyceride storage which subsequently results in reduced body fat. (125)

Catecholamines which act via adrenoreceptors are one of the major hormones controlling lipolysis in adipose tissue. Testosterone increases the beta-adrenoreceptor number. It also activates adenyl cyclase to produce cyclic adenosine monophosphate which, stimulates hormone-sensitive lipase that can accelerate lipolysis. The resultant effect is a decrease in total body fat mass(125).

There is also a direct androgen receptor mediated mechanism by which testosterone reduces adipogenesis. Pluripotent stem cells, when incubated with testosterone, developed to cells of myogenic lineage rather than adipogenic lineage. This explains the decrease in fat mass and increase in lean mass observed after testosterone therapy(126).

Proinflammatory cytokines

Testosterone improves sensitivity to insulin and reduces the production of c-reactive protein from the liver. (127). Testosterone deficiency is a proinflammatory state in which the increased fat mass leads to adipocyte dysfunction, resulting in a decrease in adiponectin . An increase in adipokines such as leptin, IL-1, IL-6, and TNF- α secreted from both adipocytes and activated macrophages which are proinflammatory is also seen in men with testosterone deficiency(128). These adipokines

can also cause systemic insulin resistance(129). Furthermore, adipokines like TNF - α also cause hypogonadism by impairing kisspeptin signalling which reduces GNRH secretion(130).

Insulin resistance

Multiple factors interplay to produce insulin resistance. The body composition, including increased adipocyte differentiation (visceral obesity) and decreased myocyte differentiation (sarcopenia) play a major role. Other factors such as increased inflammation (TNF- α , IL-1 and IL-6), decreased adiponectin and reduced mitochondrial function also contribute to insulin resistance in men with obesity(131). The resultant hyperinsulinemia due to insulin resistance acts on the kisspeptin neurons in the hypothalamus to decrease kisspeptin signalling, which, further acts on the GNRH neurons to decrease GNRH release. This will result in decreased LH secretion and thereby decreased testosterone secretion(132).

Leptin resistance

In normal human beings, low leptin levels increase release of GNRH and affect its pulsatility. High leptin levels inhibits its release. It acts through kisspeptin neurons. Testosterone usually reduces leptin production. In Obese men, there is increased release of leptins from adipocytes which unfortunately however cause central leptin resistance at the hypothalamo-pituitary level. This will in turn cause a reduction in GNRH secretion which subsequently will result in reduced LH secretion and thereby reduced testosterone secretion. (133) Increasing concentration of leptin also has an inhibitory effect on the Leydig cells in producing testosterone(134).

Final common pathway of GNRH regulation

In human brain, Kisspeptin neurons are located in the infundibular nucleus whereas GNRH neurons are situated in the preoptic area of the hypothalamus. Kisspeptin has receptor on GNRH neurons

through which it regulates the HPT-axis. GNRH neurons has kisspeptin receptors (KISS1R). They, however do not express receptors for leptin and insulin. Kisspeptin neurons, on the other hand have receptors for leptin, insulin and oestrogen. Kisspeptin neurons hence play a major role in the regulation of testosterone synthesis in the body. Leptin and insulin resistance which occurs due to obesity causes downregulation of kisspeptin neurons and this will cause reduction in production of kisspeptins. This will downregulate the GNRH secretion and causes suppression of hypothalamo-pituitary-testicular axis. Final effect is reduced testosterone synthesis.(135)

Metabolic endotoxemia

The human gut is home to more than 100 trillion bacteria and approximately 70% of these are gram negative, containing lipopolysaccharide. They produce endotoxins which is normally prevented from entering circulation by the intestinal mucosal barrier. The GELDING (Gut Endotoxin Leading to a Decline IN Gonadal function) theory, which was recently proposed suggests that high-calorie, high-fat diet can break down the integrity of the mucosal barrier and can result in metabolic endotoxemia, which is a pro-inflammatory state. This proinflammatory state can also result in hypogonadism. (136)

Obesity and sex hormone binding globulin

SHGB is a carbohydrate-rich beta-globulin protein which is produced by hepatocytes in the liver. It has high affinity to bind to testosterone and prolong the metabolic clearance of testosterone. A low SHBG level is seen in those with obesity. It is probably due to low synthesis of SHBG due to high lipid content of the liver and high pro-inflammatory cytokines (TNF-a and IL-1)(137). In addition to transporting sex steroids, SHBG has other actions including anti-inflammatory action and suppression of fat content in macrophages(138).

Hypogonadism that occurs as a result of obesity is potentially reversible. It can be managed with weight loss. A meta-analysis done by corona et al shows that body weight loss is associated with a significant increase in gonadotropins and in bound and unbound testosterone. A decline in the oestrogen level in the body was also noticed. Increase in androgen is greater in patients who lose more weight(139).

Testosterone therapy caused a statistically significant reduction in fat mass (3.5 kg, p=0.03), increase in lean body mass (2.9 kg, p=0.03) and glycated haemoglobin (Hba1c) improvement (9 mmol/mol, p=0.03), associated with 52% improvement in beta-cell function(140) . Testosterone therapy was also associated with an improvement in BMI waist circumference, lipid profile, blood pressure, lipoprotein, haemoglobin, fasting glucose, insulin resistance and leptin resistance(141). It was also observed that weight loss achieved with testosterone therapy was mainly due to loss of fat mass rather than lean body mass. On the other hand, the weight loss achieved with dieting is due to loss of both fat mass and lean body mass (142). However due to conflicting evidence relating testosterone therapy and cardiovascular disease, treatment with testosterone therapy is still controversial.

RATIONALE FOR OUR STUDY

With the latest developments in medicine, our world population is ageing. In women, the issues with post-menopausal state, the benefits and risk factors associated with hormonal therapy etc are all well-known and studied. However, there is limited data in literature on the hormonal status and its effects in elderly men. This study will help in estimating the hormonal status in men and also its association with the common health issues in elderly men. Male hypogonadism is associated with higher prevalence of cardiovascular disease, hypertension, diabetes mellitus, osteoporosis, obesity

and frailty. Since these diseases are associated with high morbidity and mortality, identification of any new risk factor and its prevalence will be useful in taking steps for prevention of these diseases.

MATERIALS AND METHODS

STUDY SETTING

The study was conducted in Christian Medical College, Vellore, a 2500 bedded academic, tertiary hospital in South India. It caters to patients who come from all over India and from various socioeconomic strata. Eligible subjects were recruited from the Geriatric out-patient clinic, which is a dedicated outpatient service for older persons. On an average, around four hundred and fifty patients attend this clinic per day.

STUDY DESIGN

Cross sectional observational study.

The study design and methods were approved by the Institutional Review Board of Christian Medical College Vellore (IRB Number: 11704)

PARTICIPANTS

Elderly men (aged 60 years or over) attending the geriatric out patient department for any complaint between January 2021 and November 2021 were recruited if they satisfied the inclusion and exclusion criteria.

INCLUSION CRITERIA

Men aged >60 years attending geriatric OPD for any indication who have given informed consent for the study

EXCLUSION CRITERIA

1. Patients who do not give consent for the study

2. Men with history of hypopituitarism

3. Patients with renal failure, liver cirrhosis, malignancy, autonomic neuropathy

4. Patients already on testosterone replacement therapy or hormonal therapy

5. Patients on anti-androgen agents, antifungal agents, or steroidal agents

6. Patients who had undergone surgical or medical therapy for benign prostate hyperplasia (BPH)

SAMPLE SIZE

The primary objective of the study was to find the prevalence of hypogonadism in elderly attending geriatric OPD. For the sample size calculation, the statistical input was taken from the following reference article "Prevalence of hypogonadism in males aged at least 45 years the HIM study "which showed a prevalence of 38.7%. The sample size was calculated using n master version 2.0.

Formula

$$n = \frac{Z^2_{1-\alpha/2}\, p\,(1-p)}{d^2}$$

Where,

p : Expected proportion

d : Absolute precision

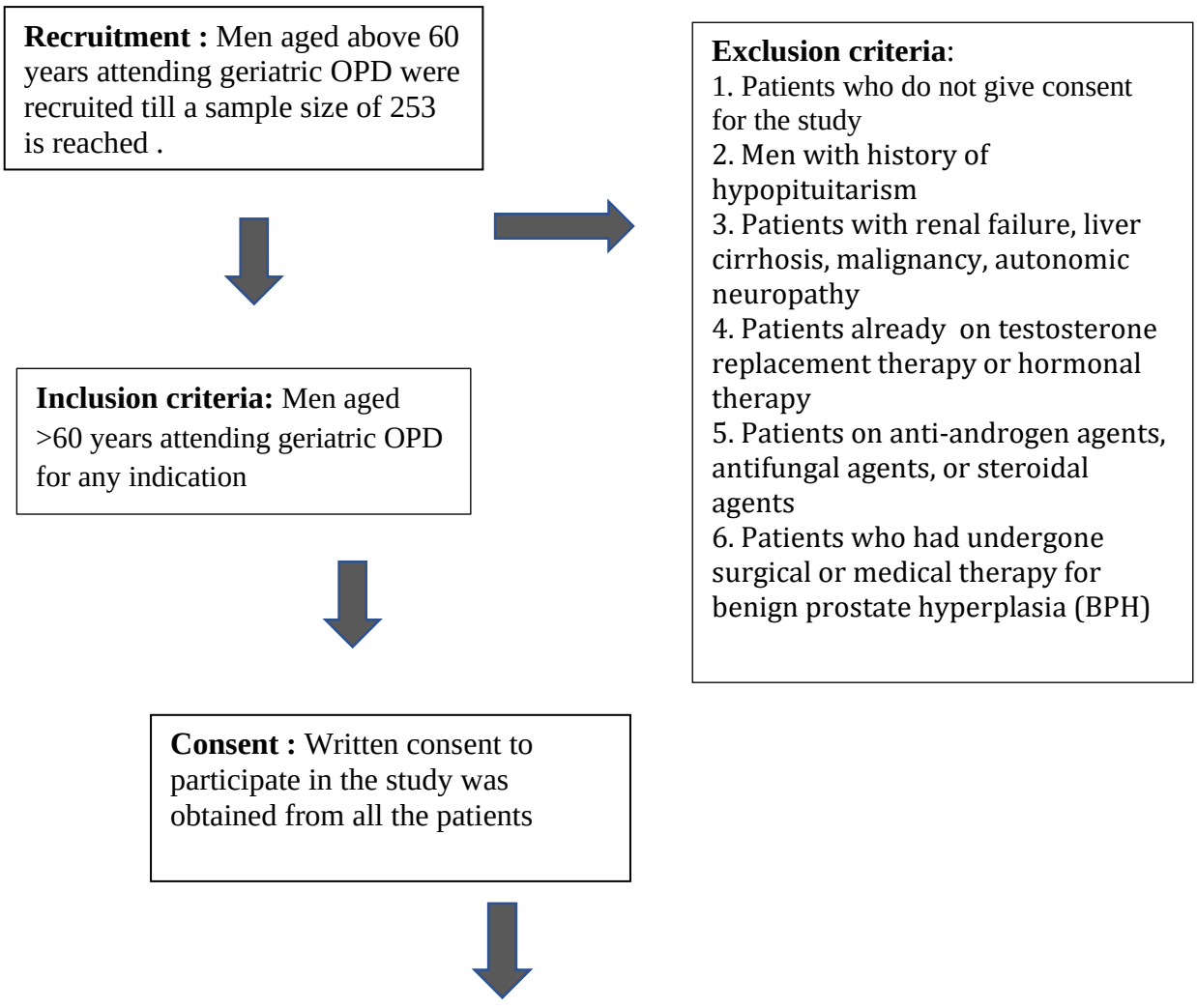
1- α/2 : Desired Confidence level

With the expected proportion of 0.387, 6% precision and 95% confidence level, the calculated sample size was 253.

SUBJECT ENROLMENT

Patients attending the geriatric OPD during the study period were screened for enrolment. If the patient fulfilled the necessary inclusion and exclusion criteria, they were approached for informed consent. If the patient consented, an interview was conducted according to the investigators proforma, clinical examination including blood pressure and gait speed were done and blood was drawn for the estimation of testosterone (total and free) levels. AC, PC, Hba1c, ECG were done as routine in geriatric OPD and the results of these were followed up. All patients were required to undergo a DEXA scan as well. Patients who spoke English, Hindi or Tamil were included, as the PI was proficient in these languages. The questionnaires were administered by the PI alone.

METHODOLOGY



-Serum testosterone levels was done on all patients
-Past history of diabetes, hypertension, cardiovascular diseases , duration of these diseases and treatment history of the same were taken.
-ADAM questionnaire was done for all the participants
- FRAIL scale was asked to all participants.
-Short physical performance battery was done.
-Physical examination including blood pressure, gait speed was done for all the patients
-Hba1c, AC, PC, ECG, DEXA scan (for osteoporosis) were done if not yet done

The prevalence of hypogonadism was calculated.
Any association of hypogonadism with diabetes mellitus, hypertension, cardiovascular diseases, osteoporosis, frailty and obesity was assessed.

VARIABLES

PRIMARY OUTCOME VARIABLE:

1. Hypogonadism

   Diagnostic criteria for hypogonadism: Men with serum testosterone levels lower than 300 ng/dl with ADAM questionnaire suggestive of signs and symptoms of low testosterone.(143)

SECONDARY OUTCOME VARIABLES:

2. Diabetes mellitus**:**

   -Blood sugar of greater than or equal to 200 mg/dl or

   -Fasting blood sugar of greater than or equal to 126 mg/dl or

   -hba1c of greater than or equal to 6.5% or

   -2 hour blood sugar of greater than or equal to 200 mg/dl or(144)

   - Patients who were already diagnosed with diabetes mellitus with the above mentioned criteria

3. Hypertension:

Chronic elevation in bp (systolic ≥140 mm hg or diastolic ≥90 mm hg), patient on medication for HTN diagnosed in the past (145)

4. Cardiovascular disease:

   ECG changes indicating ischemic heart disease, past history of myocardial infarction, history of CABG performed in the past, past history of stroke.

5. Osteoporosis:

   Bone density that falls 2.5 standard deviations (SD) below the mean for young healthy adults of the same sex, also referred to as a T-score less than <2.5. (146)

6. Frailty:

   Fried Frailty Tool

   Presence of any three of the following 5 criteria:

   1. Weight loss >5 % in the last year
   2. Exhaustion
   3. Weakness (decreased grip strength)
   4. Slow walking speed (> 6-7 seconds to walk 15 feet)
   5. Decreased physical activity assessed using a Short physical performance battery. (147)

   FRAIL scale(148):

   1. "Have you felt fatigued? Most or all of the time over the past month?"
   2. "Do you have difficulty climbing a flight of stairs?"
   3. "Do you have difficulty walking one block?"

4. “Do you have any of these illnesses: hypertension, diabetes, cancer (other than a minor skin cancer), chronic lung disease, heart attack, congestive heart failure, angina, asthma, arthritis, stroke, and kidney disease?”) Five or greater = 1, fewer than 5 = 0
5. “Have you lost more than 5 percent of your weight in the past year?”

   Frail – scores 3 to 5

   Pre-frail - 1 to 2

   Robust – 0

7. Obesity(149):

   BMI – 30 or above

STUDY OUTCOME

A diagnosis of hypogonadism in elderly men was the primary outcome measure. Hypogonadism in elderly men was defined by the following criteria:

Serum testosterone levels lower than 300 ng/dl with ADAM questionnaire suggestive of signs and symptoms of hypogonadism.

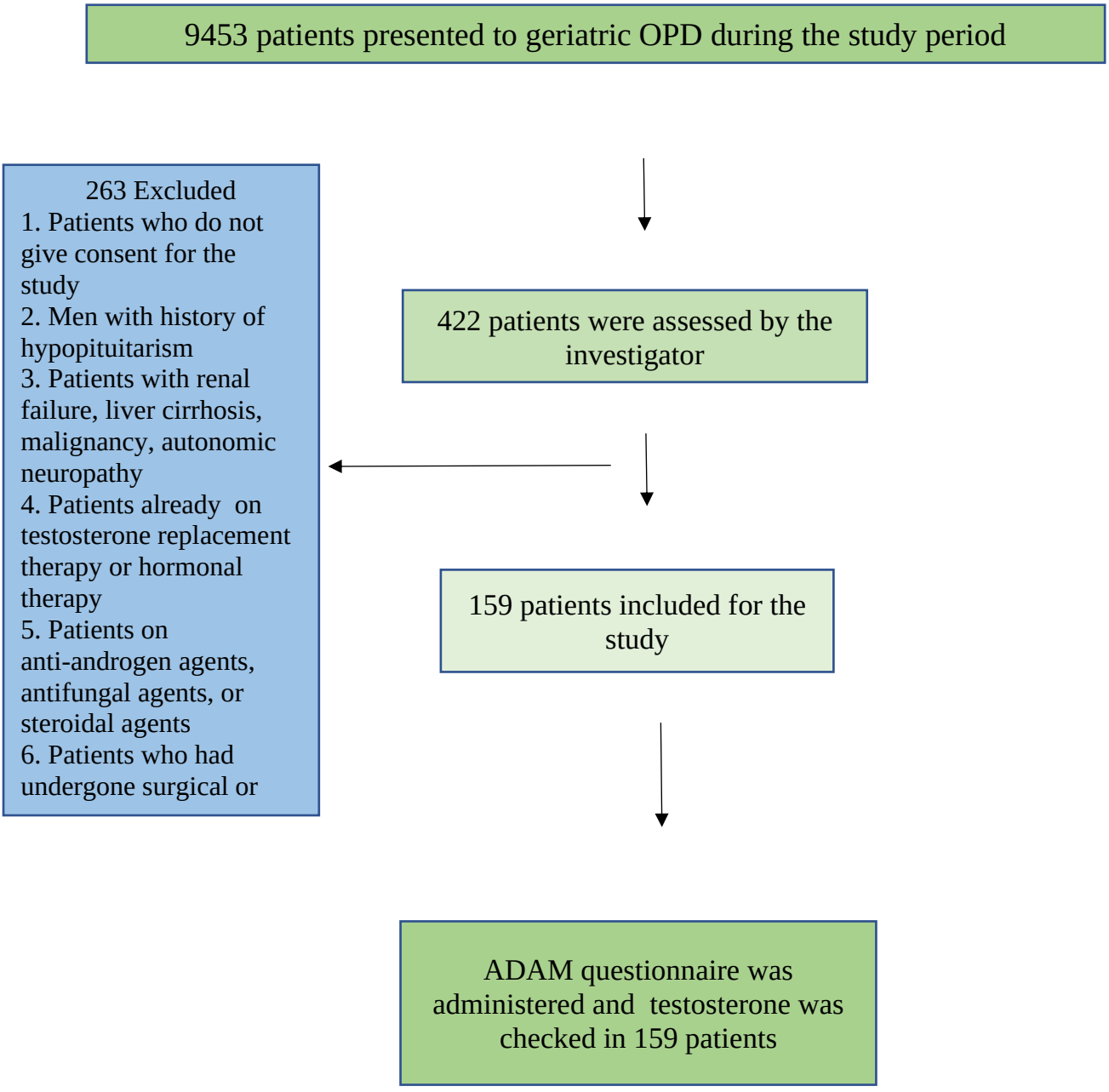
STATISTICAL ANALYSIS:

Continuous data such as age were presented with descriptive statistics were presented with n, mean and standard deviation. Non-normally distributed interval data and ordinal data were presented with median (interquartile range [IQR]) . Number of patients and percentage were presented for categorical data.

The Chi-square or Fisher’s exact test were used to find association of hypogonadism with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis and obesity. All tests were two-sided at $\alpha=0.05$ level of significance. All analyses was done using Statistical Package for Social Services (SPSS) software Version 21.0 (Armonk, NY: IBM Corp) and R v4.0

RESULTS

CONSORT DIAGRAM



ADAM -Androgen Deficiency in Aging Male

DEMOGRAPHIC CHARACTERISTICS

AGE DISTRIBUTION

The mean age of the subjects was 67.71years (SD 5.411). The median age of the subjects was 67years (IQR 64-71).

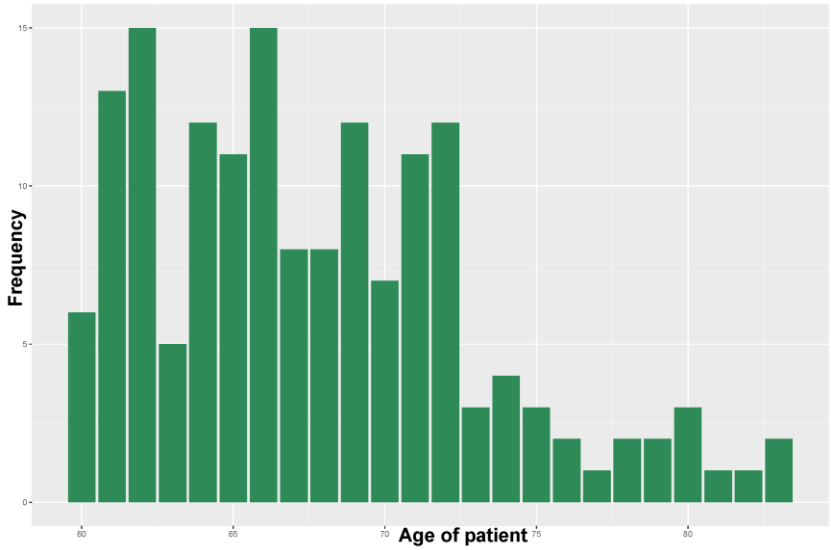


FIGURE 9:AGE DISTRIBUTION

STATE DISTRIBUTION

Subjects from different states of India were included in the study. Maximum subjects were from Tamil Nadu (56.6%).

TABLE 11: STATE DISTRIBUTION

State	Frequency	Percent
Tamil Nādu	91	56.6
West Bengal	31	19.5
Jharkhand	15	9.4
Andhra Pradesh	10	6.3
Bihar	8	5
Assam	1	0.6
Chhattisgarh	1	0.6
Tripura	1	0.6
Uttar Pradesh	1	0.6
Total	159	100

EDUCATION

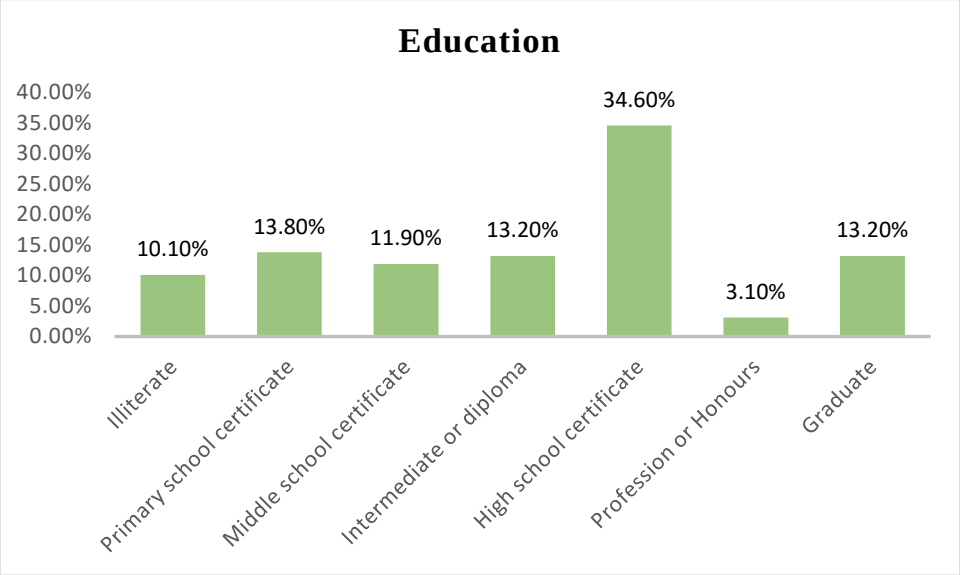


FIGURE 10: EDUCATION OF THE SUBJECTS

Majority of the study population 89.9% (143 out of 159) were literate. Only 10.1% (16) were illiterate.

OCCUPATION

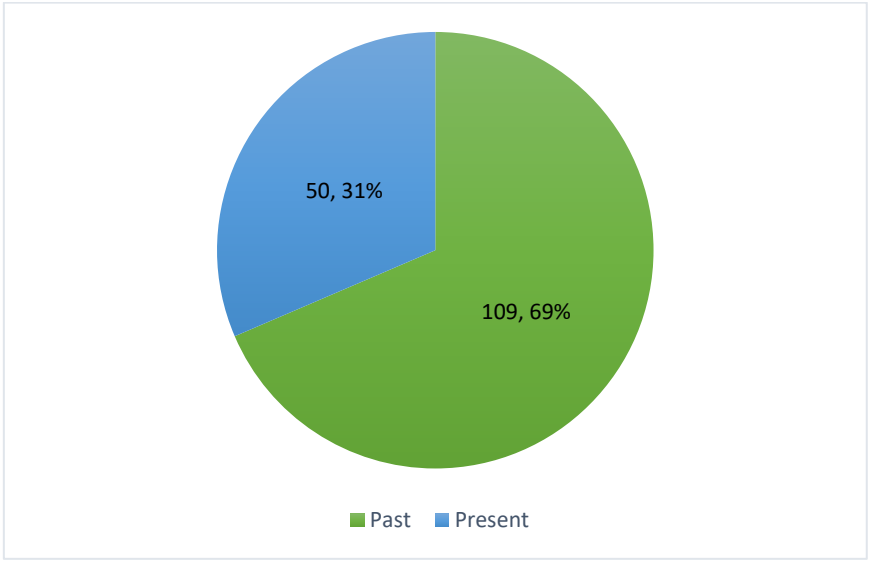


FIGURE 11: OCCUPATION OF THE SUBJECTS

Of the 159 subjects, 109(64%) were not working. Only a minority, 50(31%) participants were working. Those who had retired were considered as unemployed.

TABLE 12: OCCUPATION OF SUBJECTS

Occupation	Frequency	Percent
Unemployed	109	69
Clerks	1	0.6
Craft & Related Trade Workers	5	3.1
Elementary Occupation	19	11.9
Plant & Machine Operators and Assemblers	2	1.2
Professionals	2	1.2
Skilled Agricultural & Fishery Workers	2	1.2
Skilled Workers and Shop & Market Sales Workers	15	9.4
Technicians and Associate Professionals	4	2.5
Total	159	100.0

INCOME PER MONTH

TABLE 13: INCOME PER MONTH OF THE SUBJECTS

Income	Frequency	Percent
<2640	1	0.6
2641-7886	31	19.5
7887-13160	27	17.0
13161-19758	13	8.2
19759-26354	22	13.8
26355-52733	42	26.4
>52734	23	14.5
Total	159	100.0

The maximum number of subjects, 26.4% (42) were receiving a monthly income between Rs. 26355 and Rs. 52733.

COMORBIDITIES

DIABETES MELLITUS

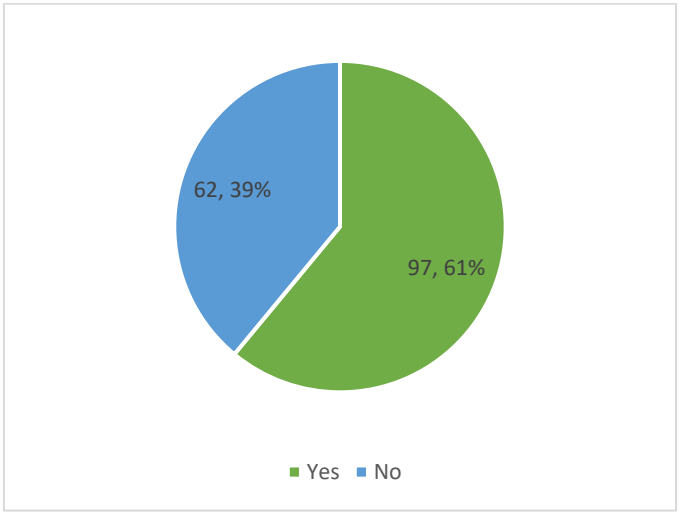


FIGURE 12: SUBJECTS WITH DIABETES MELLITUS

61% (97) of the subjects recruited had Type 2 diabetes mellitus. 90% of them were on hypoglycaemic agents. Some were on more than one oral hypoglycaemic agent. Biguanides were the most commonly used hypoglycaemic agents and Metformin was the most common medication used. 12.37% of all patients with diabetes mellitus were on insulin.

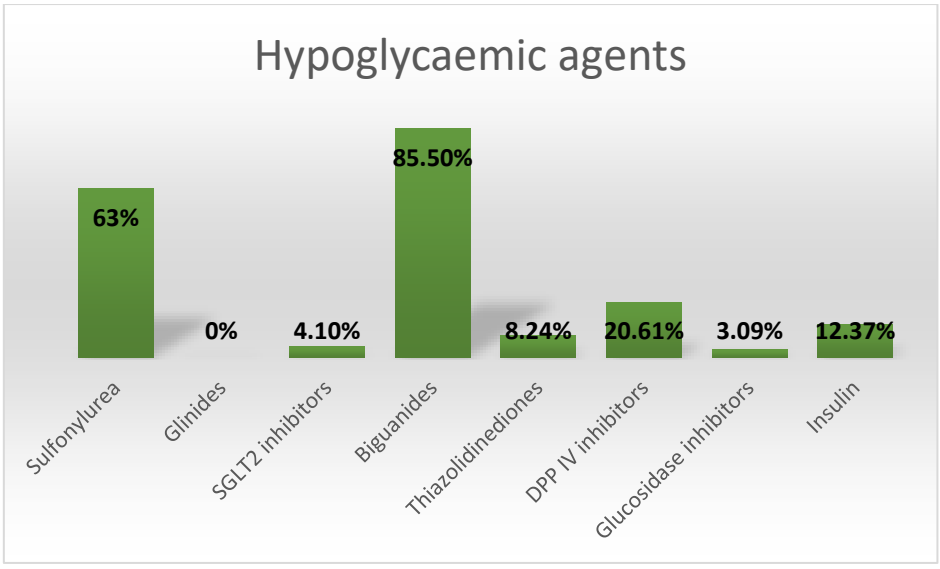


FIGURE 13: HYPOGLYCAEMICS AGENTS

SYSTEMIC HYPERTENSION

64 % (100) of the study subjects had systemic hypertension and 56 % of the subjects had hypertension for more than 5 years.

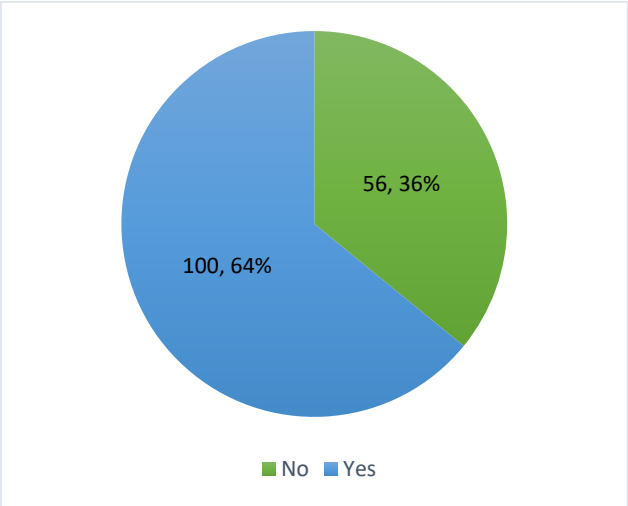


FIGURE 14: SUBJECTS WITH SYSTEMIC HYPERTENSION

All of them were on antihypertensives and many were on more than one antihypertensive agent. Most commonly used group of antihypertensive agents was calcium channel blockers (69%) followed by angiotensin receptor blockers (42%).

56 % of subjects had hypertension for more than 5 years.

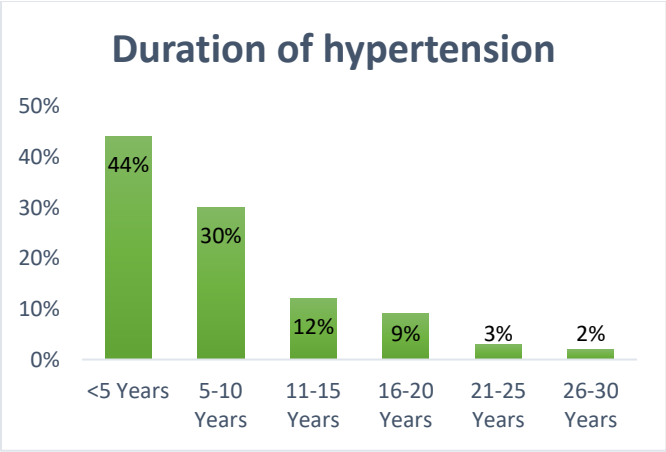


FIGURE 15: DURATION OF HYPERTENSION

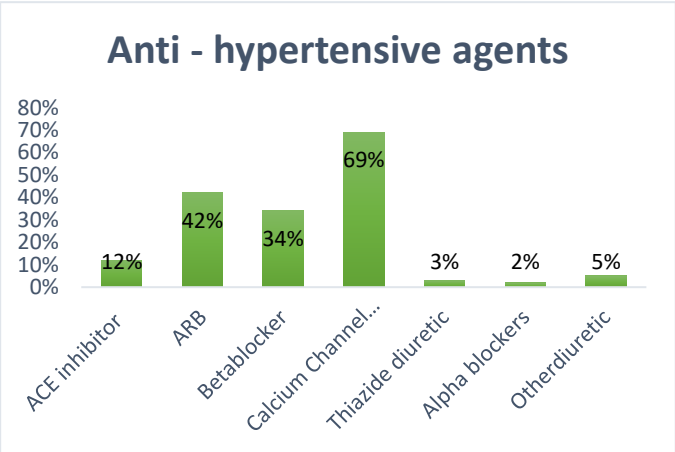


FIGURE 16: ANTIHYPERTENSIVE AGENTS

CARDIOVASCULAR DISEASES

38 (24%) subjects had cardiovascular diseases either in the form of ECG changes, previous myocardial infarction, previous CABG or cerebrovascular accidents.

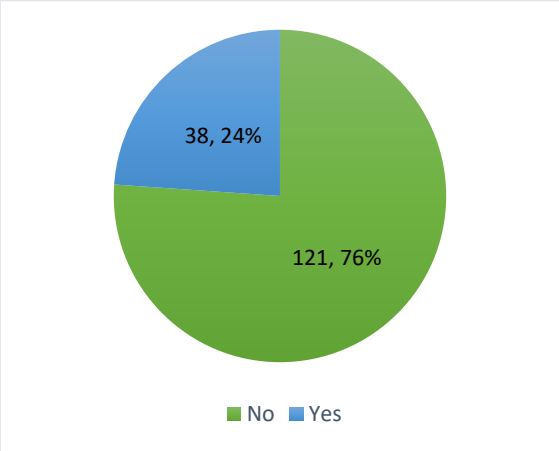


FIGURE 17: SUBJECTS WITH CARDIOVASCULAR DISEASES

23(39.4%) of them had cerebrovascular accidents and 15(60.6%) of them had cardiac diseases.

OTHER COMORBIDITIES

46.5% (74) of the patients had dyslipidaemia. The other common comorbidities the subjects had were chronic obstructive pulmonary disease (21.4%, 34) and hypothyroidism (5.7%, 9). A small percentage of patients had Parkinson disease (2.5%, 4).

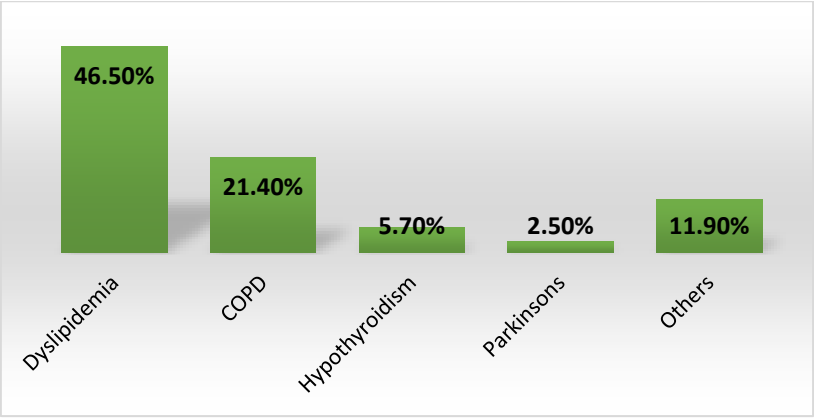


FIGURE 18: OTHER COMORBIDITIES

Other comorbidities the recruited subjects had included atrial fibrillation, osteoarthritis, obstructive sleep apnoea, filariasis, pernicious anaemia, schizophrenia, vitiligo and pernicious anaemia.

TABLE 14: OTHER COMORBIDITIES

Comorbidity	Frequency	Percentage
Atrial fibrillation	1	0.6
Heart Failure	1	0.6
Filariasis	1	0.6
OSA	1	0.6
Osteoarthritis	14	8.8
Pernicious anaemia	1	0.6
Schizophrenia	1	0.6
Vitiligo	1	0.6

OSTEOPOROSIS

Only 85 subjects underwent DEXA scan and among them, 20 % had osteoporosis in at least one of the three sites, i.e. Femoral neck, L1 vertebrae or radius.

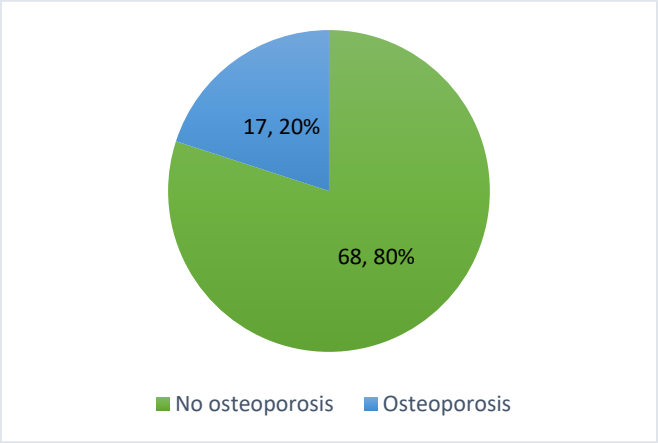


FIGURE 19: SUBJECTS WITH OSTEOPOROSIS

Among those who underwent DEXA scan, 37.6% (32), 51.2% (43) and 46.4% (39%) respectively had healthy bones in the femoral neck, L1 vertebrae and radius. 62.3%, 48.8% and 53.6% respectively had at least osteoporosis or osteopenia in the femoral neck, L1 vertebrae and radius. Though the prevalence of osteoporosis was less, osteopenia was quite prevalent among the subjects.

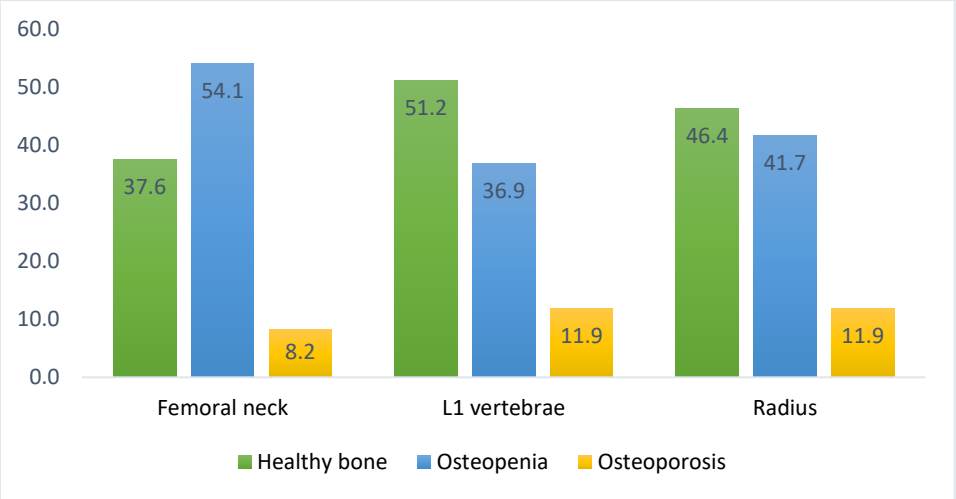


FIGURE 20: BONE HEALTH STATUS AT FEMORAL NECK, L1 VERTEBRAE AND RADIUS

BODY MASS INDEX (BMI)

The mean height of the subjects was 164.78 cm (SD 6.671) and the median height was 165 cm (IQR 160-169). The mean weight of the subjects was 68.05 Kg (SD 13.469) and median weight was 66 Kg (IQR 57.20-76.6). 50% of the subjects were either obese or overweight and 4% were underweight.

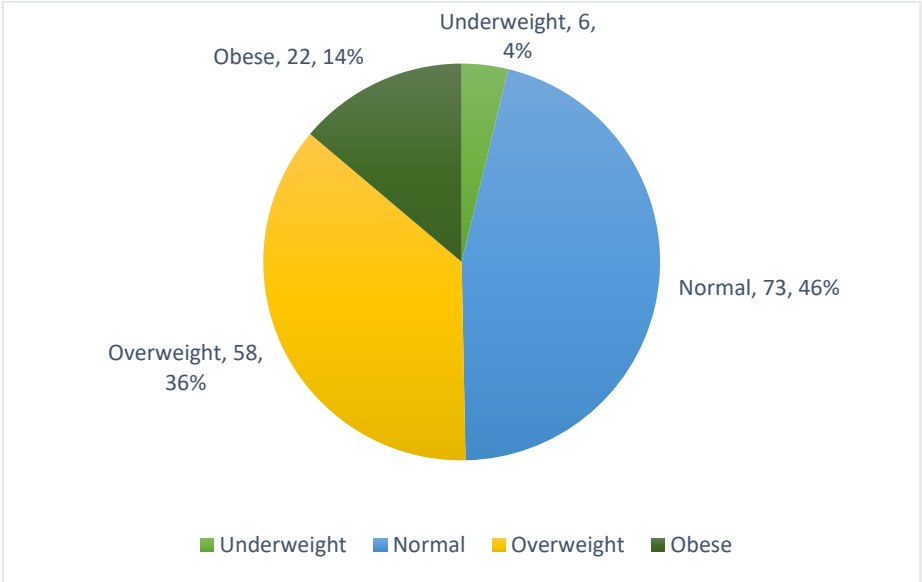


FIGURE 21: BMI CATEGORIES OF THE SUBJECTS

FRAILTY

FRAIL scale was used to identify subjects with frailty. Majority, i.e. 71%(112) of the subjects were robust and 29%(47) were either frail or pre-frail.

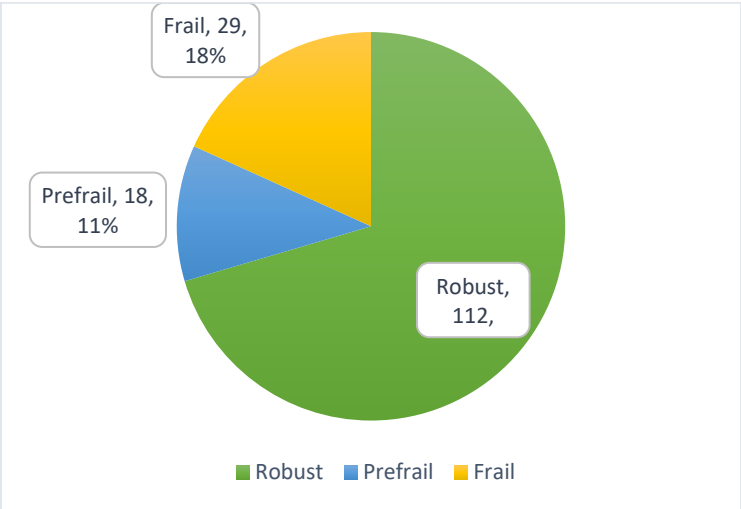


FIGURE 22: FRAIL, PRE - FRAIL AND ROBUST SUBJECTS

ADDICTIONS

40.3% (64) subjects were smokers. Only 7.5 % was currently smoking. 35.2 % (58) subjects have consumed alcohol and 9.4% were currently consuming alcohol.

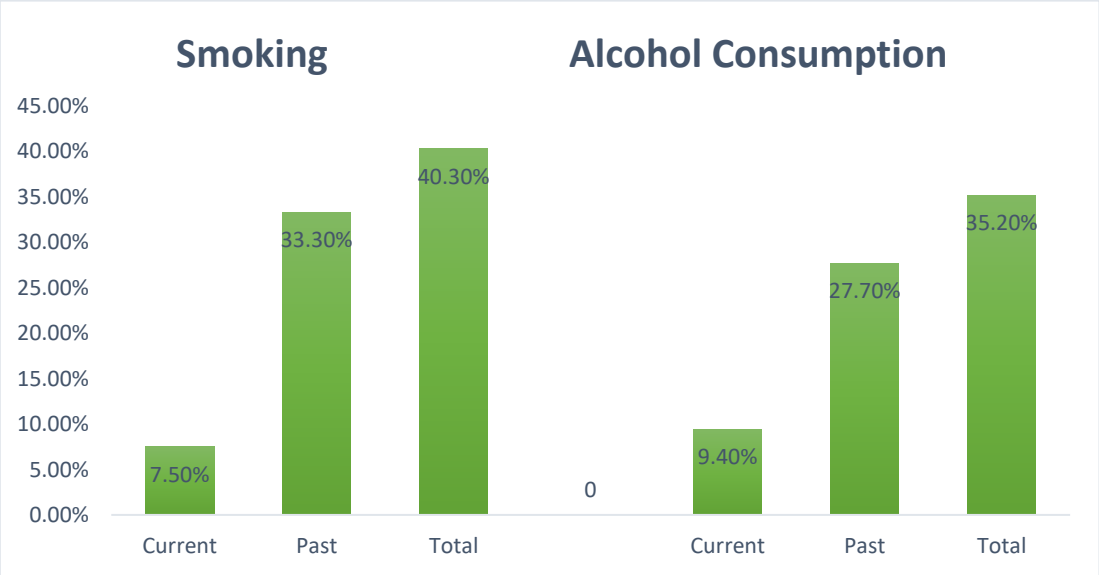


FIGURE 23: FREQUENCY OF SMOKING AND ALCOHOL CONSUMPTION IN SUBJECTS

Around 23 % had history of smoking for >40 pack years and 25% had history of alcohol consumption for >30 years.

TABLE 15: DURATION OF SMOKING AND ALCOHOL CONSUMPTION

Smoking pack years	Frequency	Percent		Alcohol duration	Frequency	Percent
<10 Years	12	18.8		<10 Years	5	8.6
10-20 Years	12	18.8		10-20 Years	13	22.4
20-30 Years	10	15.6		20-30 Years	15	25.9
30-40 Years	15	23.4		30-40 Years	22	37.9
>=40 Years	15	23.4		>=40 Years	3	5.2

The other common addiction was chewing tobacco (30, 18.9%).

ADAM QUESTIONNAIRE

The ADAM questionnaire was administered to all the subjects and it was positive in 128(80.5%) subjects.

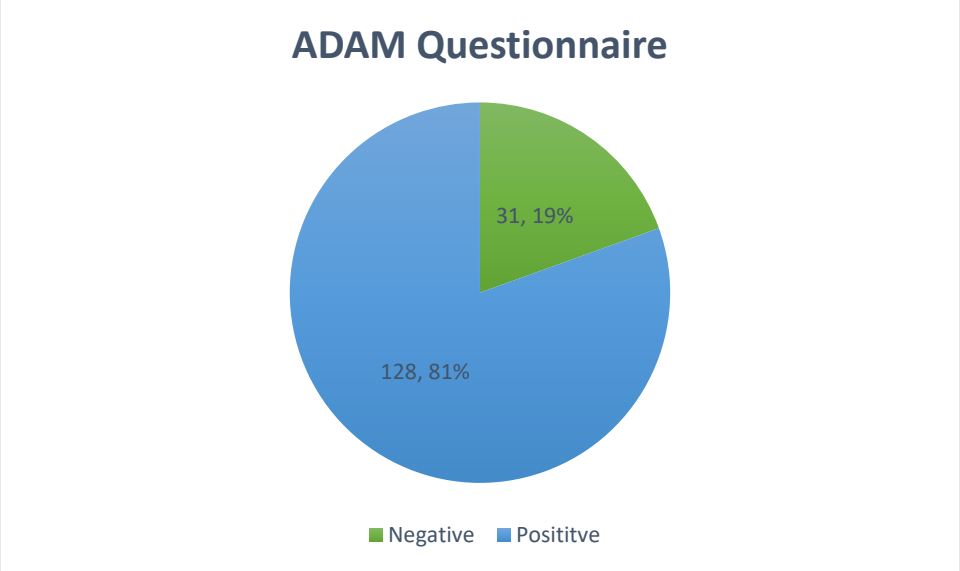


FIGURE 24: SUBJECTS WHO GAVE POSITIVE ANSWER TO ADAM QUESTIONNAIRE

LABORATORY PARAMETERS

Total testosterone, free testosterone, SHBG, Albumin, Bioavailable testosterone and Free testosterone index were checked in all subjects. The mean total testosterone was 297.616 ng/dL (SD 148.42) and median total testosterone was 262 ng/dL (IQR 200 ng/dl- 377ng/dL).

TABLE 16: LABORATORY PARAMETERS

		Total testosterone (Normal - >300ng/dL)	Free testosterone index (Normal – 30-50)	SHBG (10-57nmol/L)	Free testosterone (>5 ng/dL)	Bioavailable testosterone (40-168ng/dL)
Mean		297.6168	25.086	46.5211	4.78243	81.57
Std. Deviation		148.42773	19.60774	23.37267	2.273662	46.774
Median		262	22.79	39.81	4.57	81
Percentiles	25	200	18.065	29.535	3.58	41
	50	262	22.79	39.81	4.57	81
	75	377	28.275	60.955	5.65	122
Minimum		20	1.66	12.04	0.598	1
Maximum		1133	233	194	21.9	162

PRIMARY OUTCOME

PREVALENCE OF HYPOGONADISM

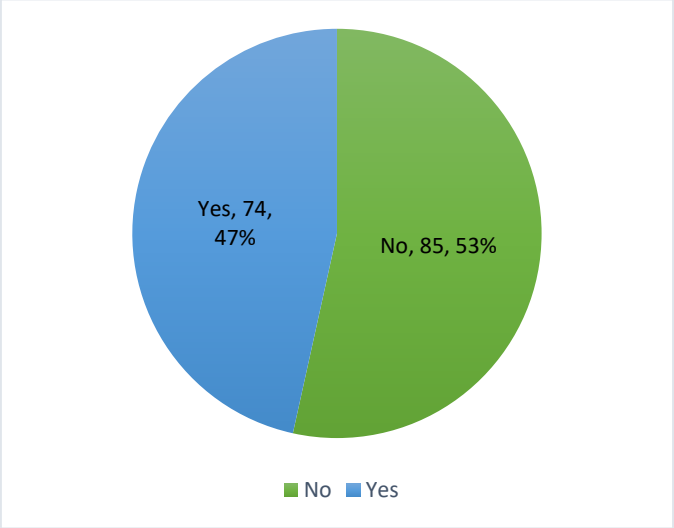
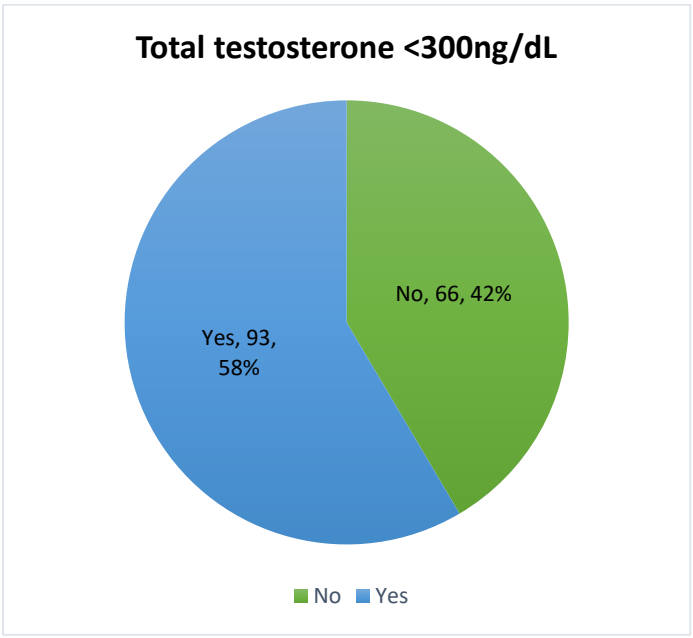


FIGURE 25: PREVALENCE OF HYPOGONADISM

Subjects with symptoms of hypogonadism, i.e. Positive ADAM questionnaire and serum total testosterone <300ng/dl were considered to have hypogonadism. In this study, the prevalence of hypogonadism was 47% (74). The laboratory prevalence of hypogonadism was higher with 58% of the subjects having total testosterone <300 ng/dl. On taking free testosterone cut off of 5 ng/dl, the prevalence of hypogonadism was even higher at 61%.



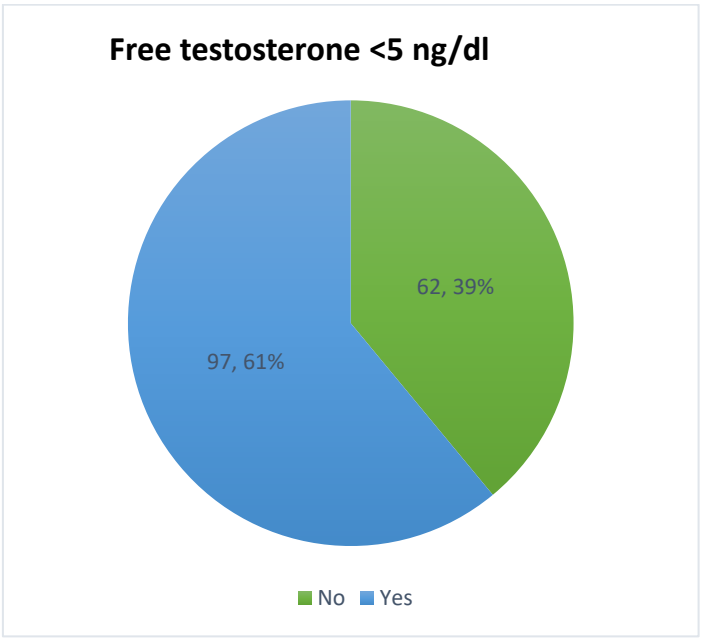


FIGURE 26:TOTAL TESTOSTERONE <300NG/DL *FIGURE 27:FREE TESTOSTERONE <5 NG/DL*

HYPOGONADISM AND AGE

Though there was no statistically significant association between age and total testosterone, when symptoms of hypogonadism were also taken into consideration along with total testosterone, there was a statistically significant association (p value 0.035).

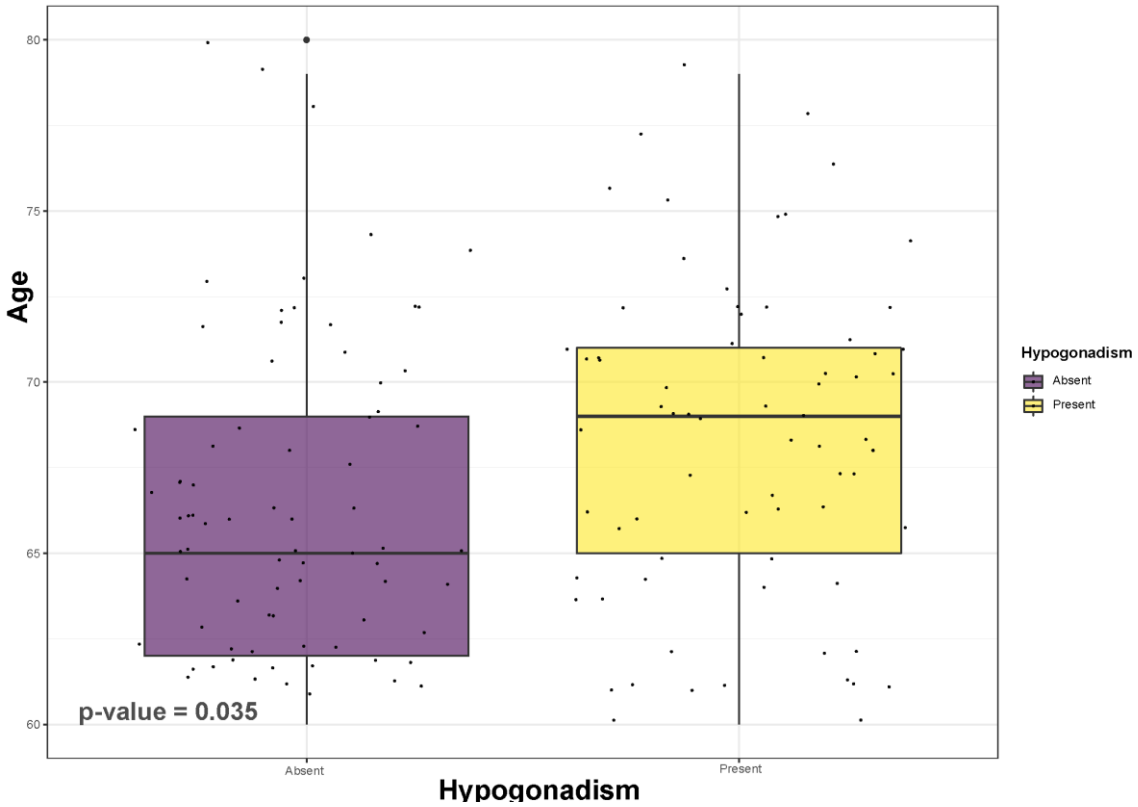


FIGURE 28: ASSOCIATION OF AGE WITH HYPOGONADISM

TOTAL TESTOSTERONE AND AGE

As age increased total testosterone showed a downward trend. However the p value was 0.3742(R squared 0.071)and it was not statistically significant.

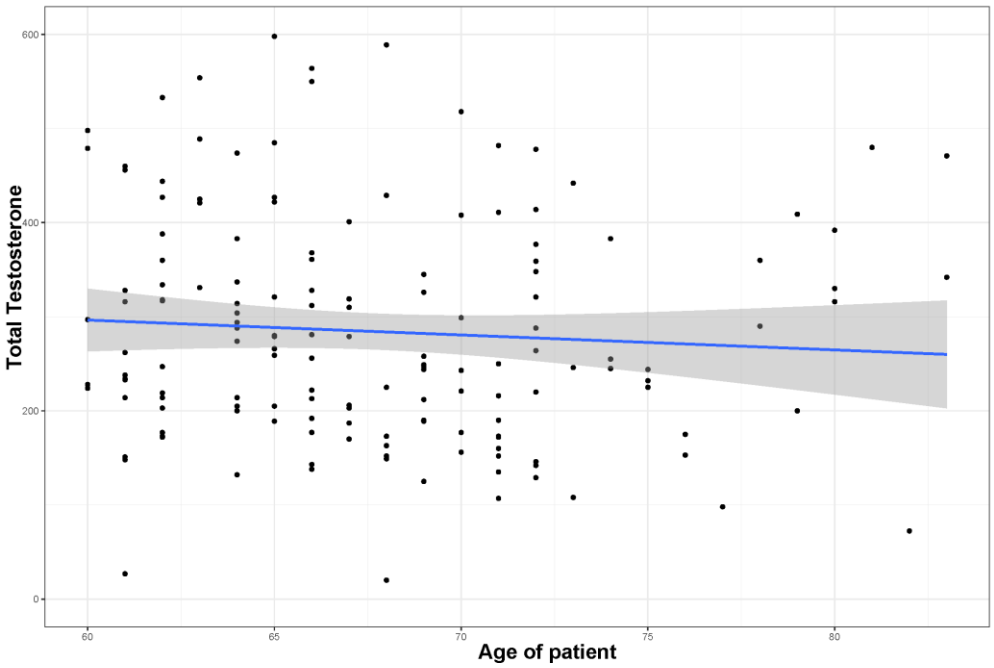


FIGURE 29: ASSOCIATION OF AGE WITH TOTAL TESTOSTERONE

FREE TESTOSTERONE AND AGE

As age increased, there was a statistically significant reduction in the free testosterone with a p value of 0.0034(r squared – 0.232)

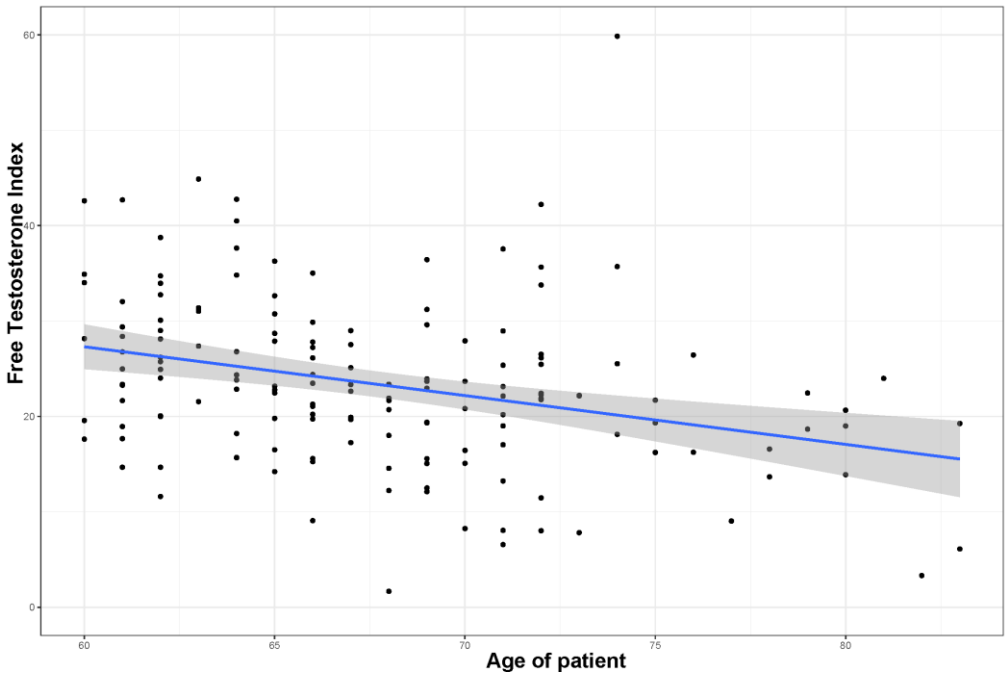


FIGURE 30: ASSOCIATION OF FREE TESTOSTERONE WITH AGE

SHBG AND AGE

The sex hormone binding globulin increased with age. It was statistically significant with a p value of 0.0002.

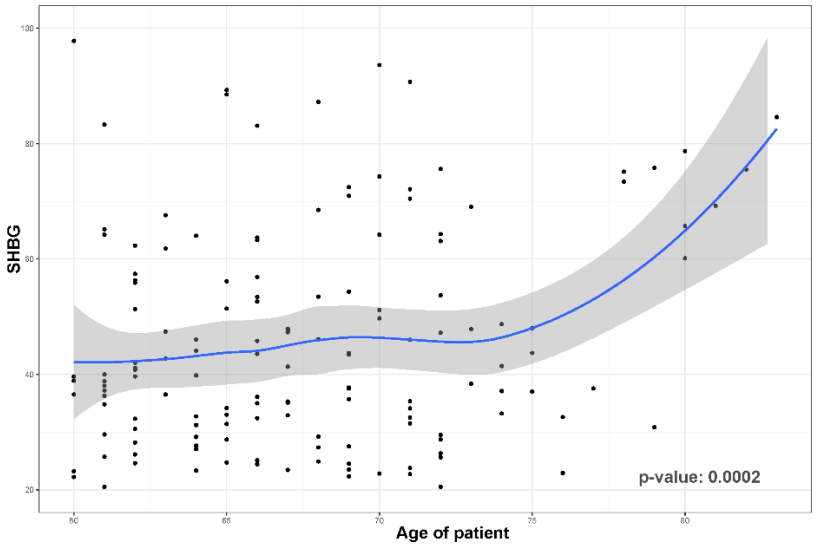


FIGURE 31: ASSOCIATION OF SHBG WITH AGE

BIOAVAILABLE TESTOSTERONE AND AGE

The bioavailable testosterone was found to decrease as age increased. It was statistically significant with a p value of 0.0056

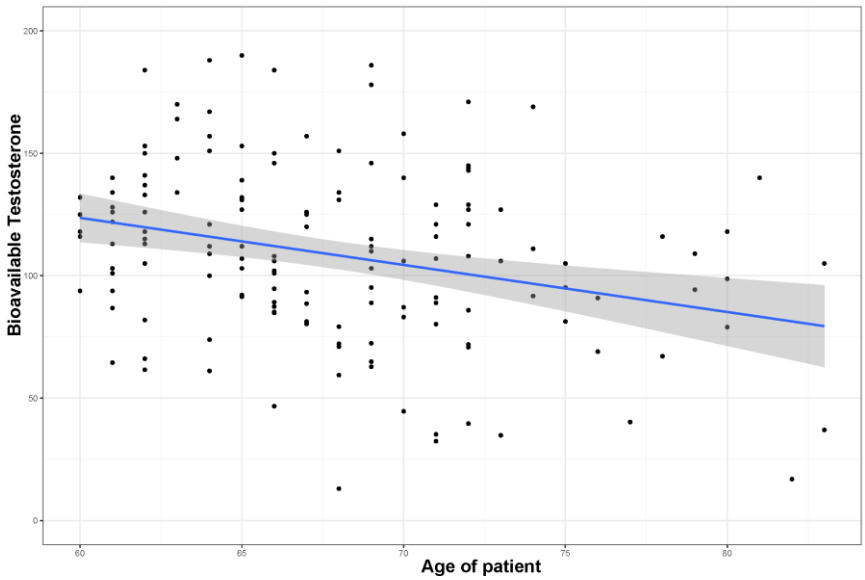


FIGURE 32: ASSOCIATION OF BIOAVAILABLE TESTOSTERONE WITH AGE

FREE TESTOSTERONE INDEX AND AGE

Free testosterone index was found to reduce as the age increased. It was statistically significant with a p value of 0.011

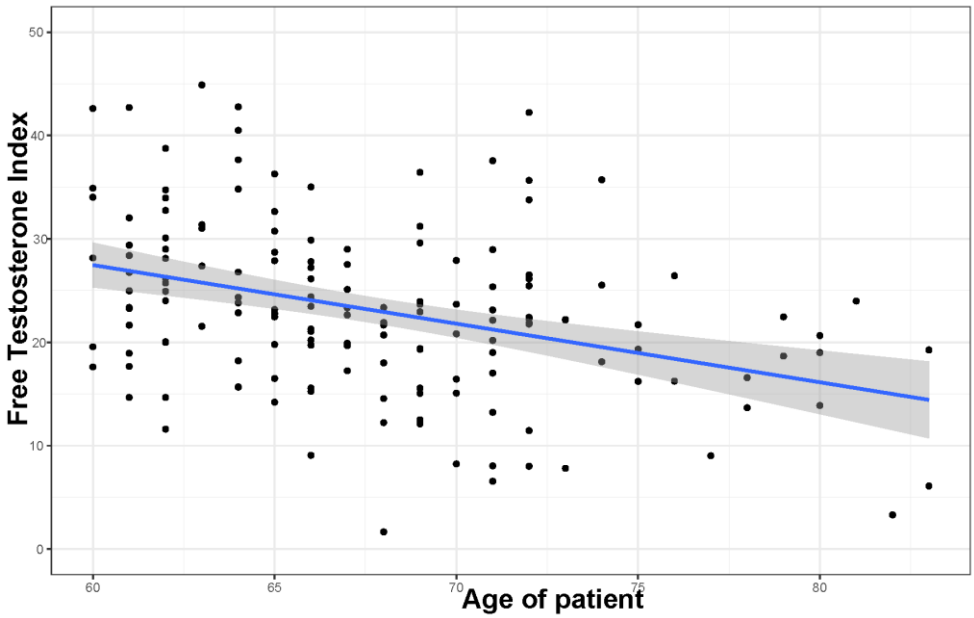


FIGURE 33: ASSOCIATION OF FREE TESTOSTERONE INDEX WITH AGE

ASSOCIATION OF HYPOGONADISM WITH COMORBIDITIES

Our study also looked into the association of hypogonadism and the comorbidities commonly seen in elderly. Hypogonadism was defined as total testosterone <300 ng/dL along with a positive ADAM score. We also assessed the association of total testosterone <300 ng/dL and free testosterone <5 ng/dL with these comorbidities.

HYPOGONADISM AND TYPE 2 DIABETES MELLITUS

There was a significant association between Diabetes Mellitus and hypogonadism with a p value of 0.025(Odds ratio 2.101, CI 1.091 - 4.047). The total testosterone value was also found to be low when the patient had diabetes mellitus. This association was significant with a p value of 0.012.

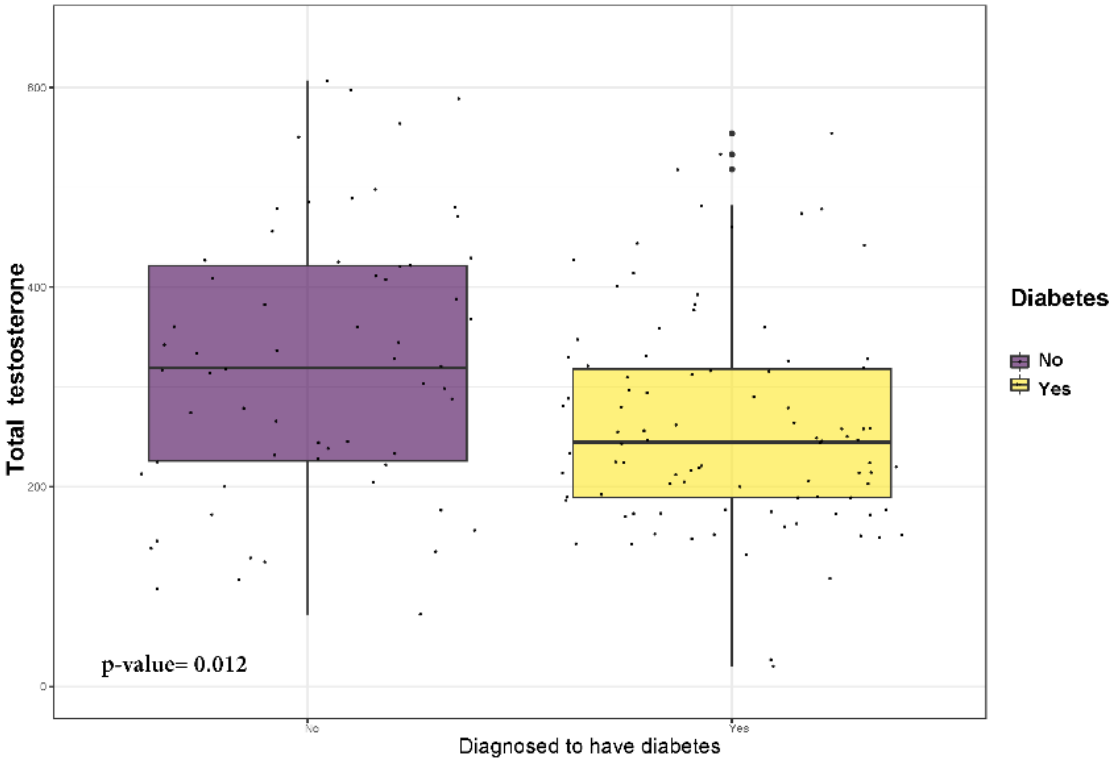


FIGURE 34: ASSOCIATION OF TOTAL TESTOSTERONE WITH DIABETES MELLITUS

Free testosterone however did not show a statistically significant association with diabetes mellitus with a p value of 0.052 even though there was a low free testosterone in subjects with diabetes mellitus.

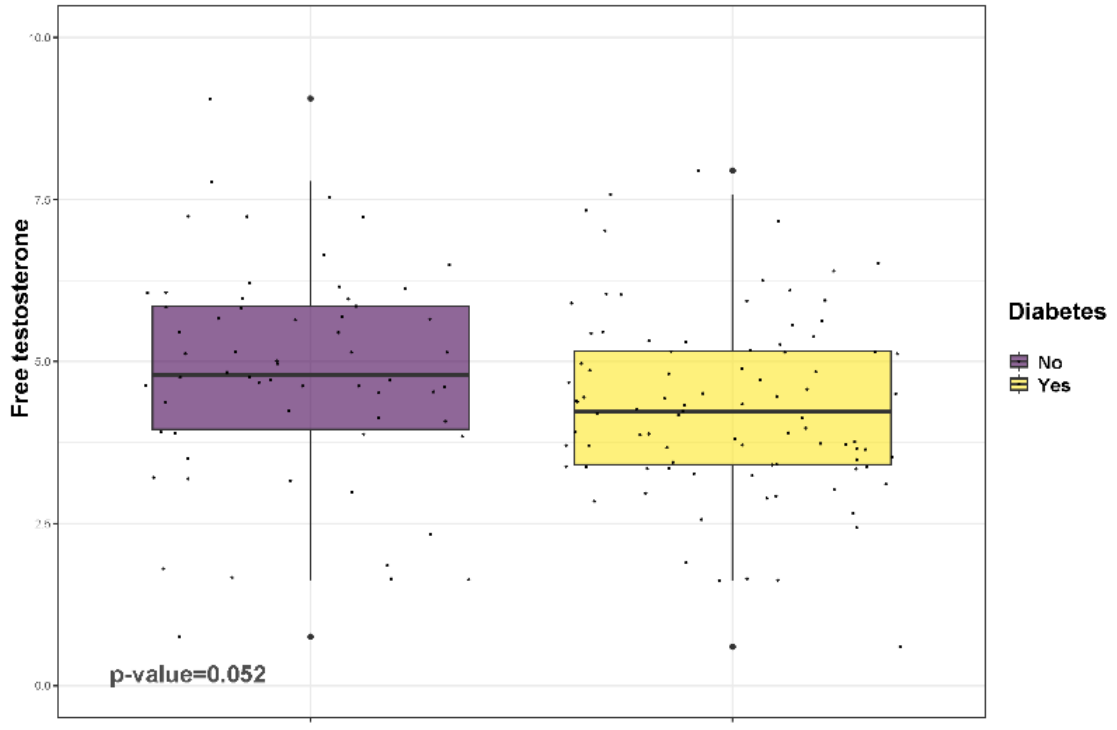


FIGURE 35: ASSOCIATION OF FREE TESTOSTERONE WITH DIABETES MELLITUS

Duration of diabetes mellitus also did not have a significant association with hypogonadism, serum testosterone or free testosterone as the p values were 0.056, 0.7253 and 0.5698 respectively.

The association of the various drugs used in diabetes with serum testosterone was also looked into and there was no significant association found.

TABLE 17: ASSOCIATION OF TOTAL TESTOSTERONE WITH HYPOGLYCAEMIC AGENTS

Hypoglycaemic agents	Association with total testosterone
Sulphonylureas	0.118
Biguanides	0.006
SGLT 2 Inhibitors	0.142
Thiazolidinediones	1
DPP IV Inhibitors	0.051
Glucosidase inhibitors	0.267
Insulin	0.745

HYPOGONADISM AND HYPERTENSION

There was no significant association between hypogonadism and hypertension. The p value was 0.461(Odds ratio 1.281, CI 0.663-2.475). Though subjects with hypertension had a low average total testosterone, it was not statistically significant(p value 0.077).

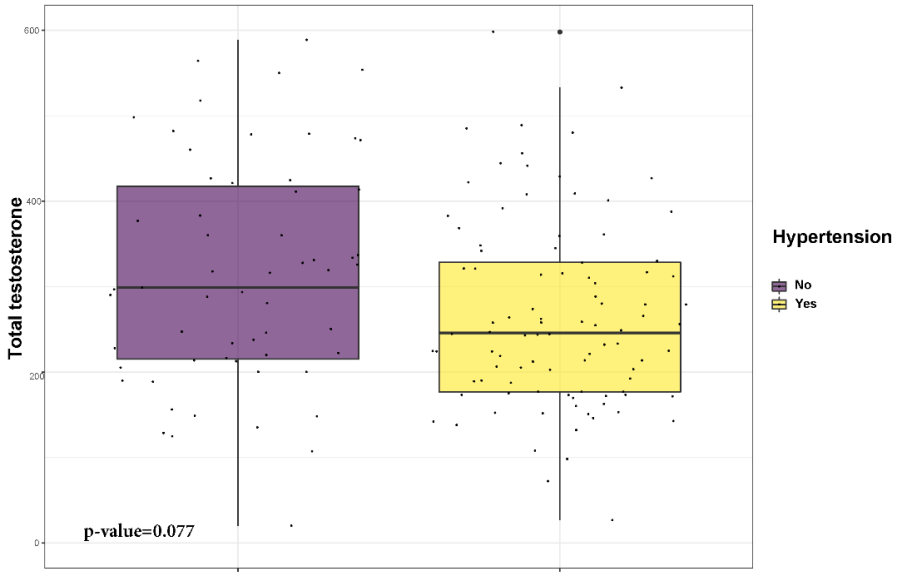


FIGURE 36: ASSOCIATION OF TOTAL TESTOSTERONE WITH HYPERTENSION

Similarly, free testosterone was also slightly lower in the group with hypertension, but it was also not statistically significant (p value- 0.127).

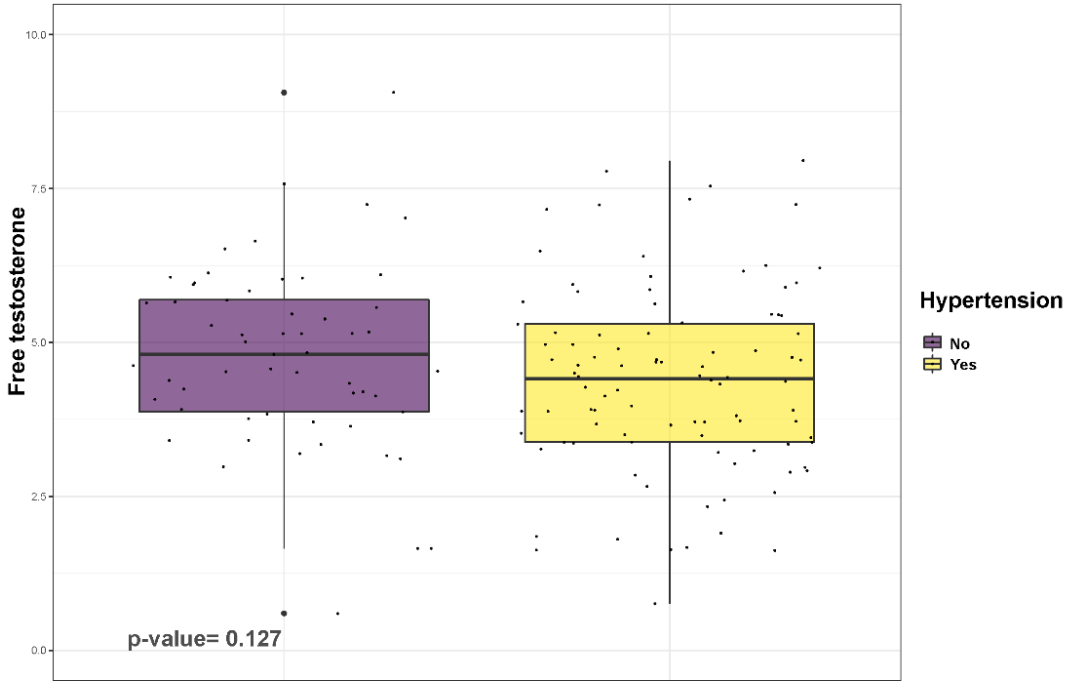


FIGURE 37: ASSOCIATION OF FREE TESTOSTERONE WITH HYPERTENSION

Duration of hypertension was also not associated with hypogonadism (p value – 0.6), total testosterone(p value – 0.325) or free testosterone(p value - 0.816). The antihypertensive drugs including ACE inhibitors, beta blockers and calcium channel blockers were found to have a statistically significant association with total testosterone with p values of 0.015, 0.016 and 0.031 respectively. Association with alpha blockers, thiazide diuretic and other diuretics were not calculated as only a small number of subjects were taking these drugs.

TABLE 18: ASSOCIATION OF TOTAL TESTOSTERONE WITH ANTI-HYPERTENSIVE AGENTS

Anti-hypertensives	Association with serum testosterone <300(p value)
ACE Inhibitor	0.015
ARBs	0.874
Beta Blocker	0.016
Calcium channel blockers	0.031

HYPOGONADISM AND CARDIOVASCULAR DISEASE

There was no statistically significant association between hypogonadism and cardiovascular diseases (p value – 0.232, odd ratio 1.562, CI 0.750-3.253). Serum testosterone and hypogonadism was also not statistically significant with a p value of 0.072.

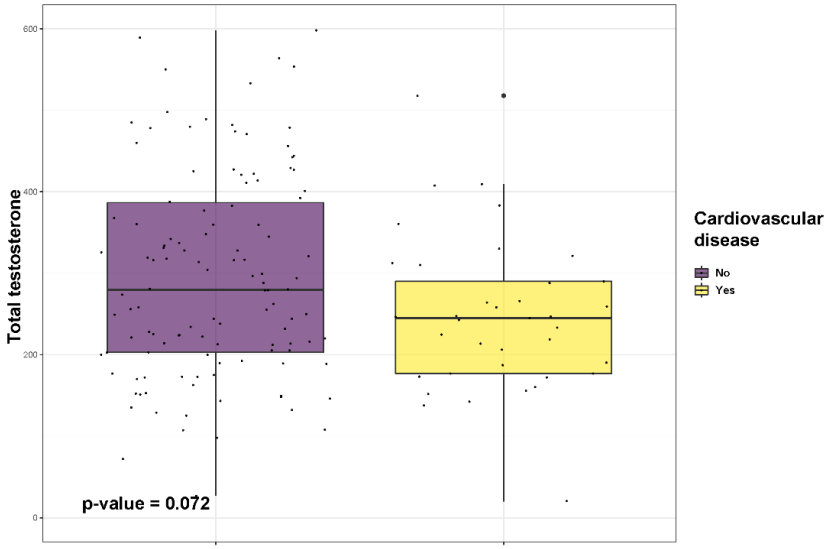


FIGURE 38: ASSOCIATION OF TOTAL TESTOSTERONE WITH CARDIOVASCULAR DISEASE

Free testosterone and cardiovascular disease also did not have any significant association (p value – 0.136).

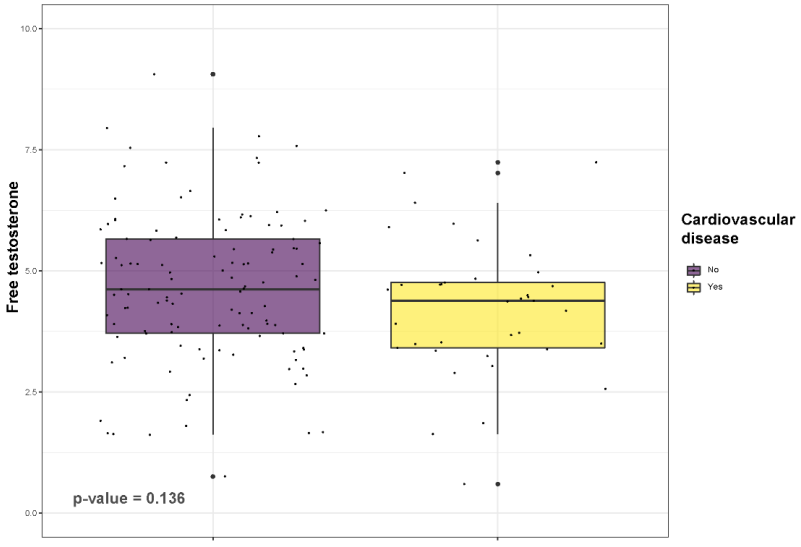


FIGURE 39: ASSOCIATION OF FREE TESTOSTERONE WITH CARDIOVASCULAR DISEASE

There was no statistically significant association between hypogonadism and cardiac diseases(excluding cerebrovascular disease) also with a p value of 0.912(odds ratio 0.958, CI 0.451-2.034). Serum total testosterone and cardiac disease also did not have any significant association(p value- 0.171, OR 1.739, CI 0.784 – 3.858). However, there was a statistically significant association between free testosterone and cardiac diseases (p value of 0.009,OR 3.188, CI 1.295- 7.849). Cerebrovascular accidents were also not associated with hypogonadism (p value- 0.283, OR 1.800, CI 0.609-5.323). Serum testosterone and free testosterone were also not statistically associated with cerebrovascular diseases with p values of 0.518 and 0.318 respectively.

HYPOGONADISM AND OTHER COMORBIDITIES

Among the other comorbidities that the subjects had, dyslipidaemia had a statistically significant association with hypogonadism (P value - 0.016, (OR 2.174, CI 1.151-4.105) and total testosterone (P value 0.005). Dyslipidaemia was however not associated with free testosterone (P value 0.209, (OR 1.511, CI 0.793- 2.879). Other comorbidities including Obstructive airway disease, Hypothyroidism and Parkinson disease did not have any association with hypogonadism, total testosterone or free testosterone.

TABLE 19:ASSOCIATION OF HYPOGONADISM, TOTAL TESTOSTERONE AND FREE TESTOSTERONE WITH COMORBIDITIES

Comorbidities	Association with hypogonadism	Association with total testosterone	Association with free testosterone
Dyslipidaemia	P value - 0.016 (OR 2.174, CI 1.151-4.105)	P value 0.005	P value 0.209 (OR 1.511, CI 0.793- 2.879)
Obstructive airway disease	P value – 0.399 (OR 1.386, CI 0.648- 2.964)	P value 0.407	P value 0.618 (OR 1.22, CI 0.555-2.691)
Hypothyroidism	P value – 0.577 (OR 1.467, CI 0.379-5.680)	P value 0.736	P value 0.730 (OR 0.788, CI 0.203-3.056)

Parkinson disease	P value – 0.248 (OR 3.549, CI 0.361- 34.879)	P value 0.642	P value 0.561 (OR 1.947, CI 0.198-19.148)

HYPOGONADISM AND OSTEOPOROSIS

Subjects were considered to have osteoporosis if they had osteoporosis at either of the three sites checked, i.e. femoral neck, L1 vertebrae or radius. Hypogonadism was not significantly associated with osteoporosis (p value 0.373, OR 0.595, CI 0.189-1.879). Hypogonadism did not have any significant association with either osteopenia or osteoporosis at any site also (p value 0.688, OR 1.238, CI 0.436-3.518).

Total testosterone was higher in subjects with osteoporosis and this association was significant with a p value of 0.017. This contradictory result might be due to the high prevalence of obese and overweight subjects with low testosterone. Obese and overweight subjects are less likely to have osteoporosis. On multivariate analysis to assess the effect of BMI on osteoporosis, we found that the results were not significant(p value of 0.077).

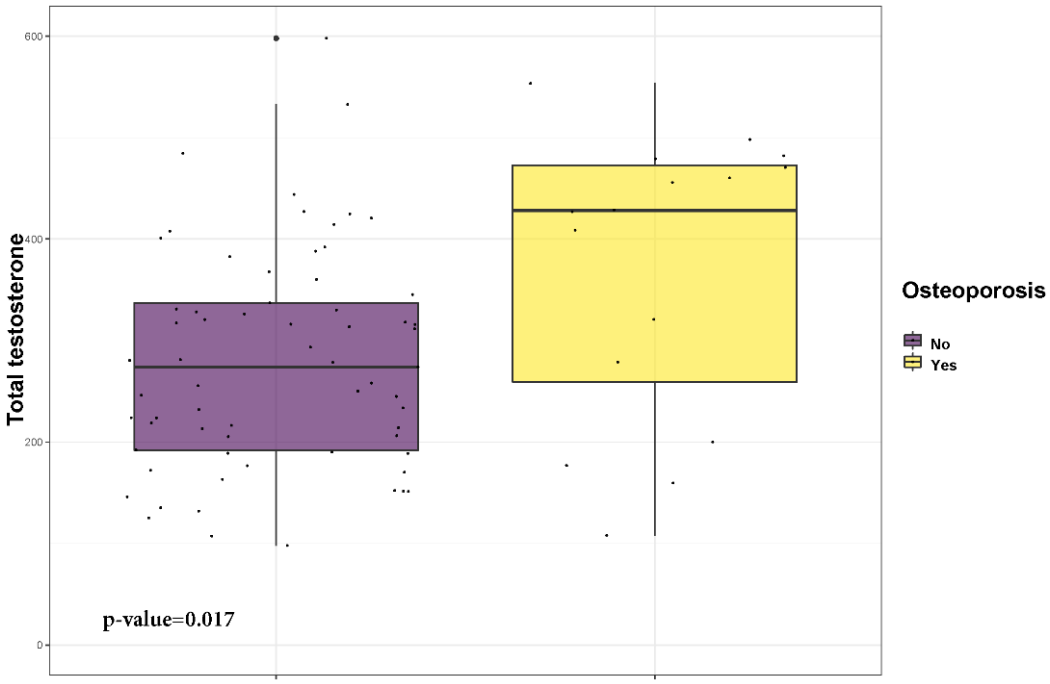


FIGURE 40: ASSOCIATION OF TOTAL TESTOSTERONE WITH OSTEOPOROSIS

Free testosterone however was not associated with osteoporosis (p value 0.943). This was also probably because of the association of free testosterone with obesity. Even though total testosterone is low, free testosterone is not as low in those with obesity.

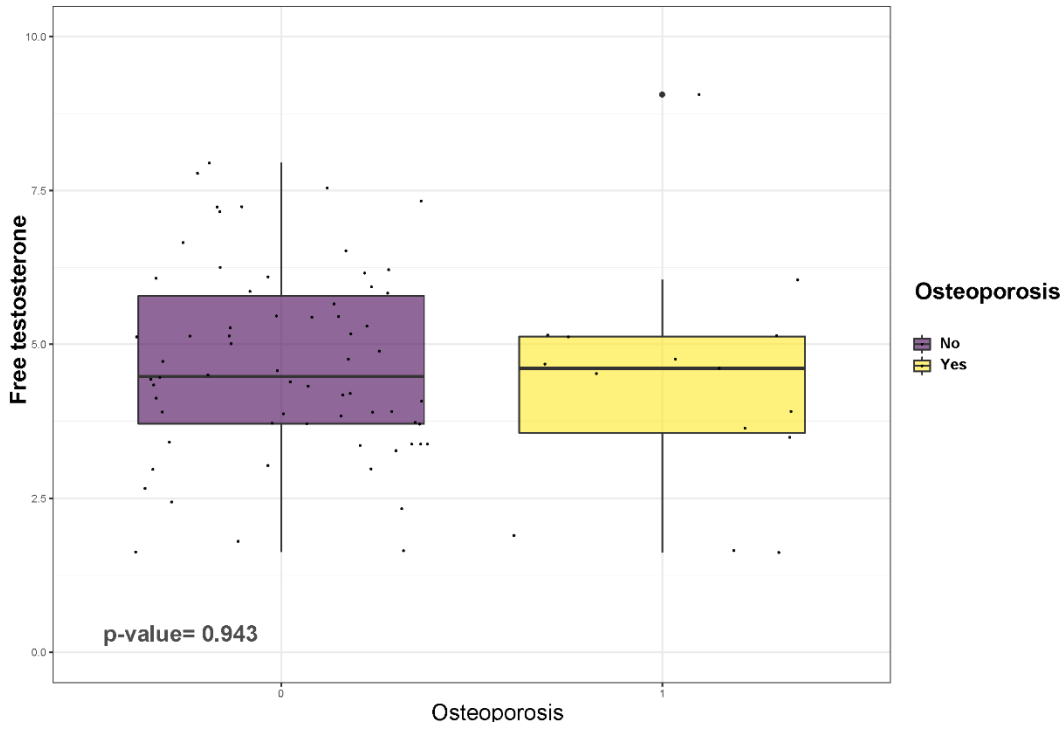


FIGURE 41: ASSOCIATION OF FREE TESTOSTERONE WITH OSTEOPOROSIS

The association of hypogonadism , total testosterone and free testosterone at different sites where Bone mineral density was checked is given in table 20. There was no significant association found at any site.

TABLE 20: ASSOCIATION OF OSTEOPOROSIS WITH HYPOGONADISM, TOTAL TESTOSTERONE AND FREE TESTOSTERONE AT DIFFERENT SITES

BMD sites	Association with Hypogonadism	Association with Total testosterone	Association with free testosterone
Femoral Neck	P value 0.561 OR 0.606, CI 0.111-3.324	P value 0.250 OR 0.380, CI 0.069-2.078	P value 0.448 OR 0.550, CI 0.115-2.625
L1 Vertebrae	P value 0.183 OR 0.347, CI 0.060-1.747	P value 0.052 OR 0.224, CI 0.045-1.128	P value 0.243 OR 0.455, CI 0.118-1.749
Radius	P value 0.522 OR 0.629, CI 0.15 -2.626	P value 0.205 OR 0.406, CI 0.097-1.692	P value 0.627 OR 0.721, CI 0.192-2.706

Association of hypogonadism , free testosterone and total testosterone with osteoporosis + osteopenia at femoral neck, L1 vertebrae and radius were also looked into and the results of the same are represented in the following table . There was no significant association found.

TABLE 21: ASSOCIATION OF HYPOGONADISM , TOTAL TESTOSTERONE AND FREE TESTOSTERONE WITH OSTEOPOROSIS + OSTEOPENIA

BMD sites	Association with Hypogonadism	Association with Total testosterone	Association with free testosterone
Femoral Neck	P value 0.469 OR 0.718, CI 0.293-1.76	P value 0.327 OR 0. 644, CI 0.266-1.557	P value 0.166 OR 1.870, CI 0.169-4.550
L1 Vertebrae	P value 0.346 OR 0.655, CI 0.271-1.583	P value 0.188 OR 0.561, CI 0.236-1.332	P value – 0.801 OR 1.118, CI 0.471-2.654
Radius	P value 0.761 OR 0.873, CI 0.363-2.099	P value 0.988 OR 1.007, CI 0.427-2.374	P value 0.574 OR 1.286, CI 0.540-3.060

HYPOGONADISM AND BODY MASS INDEX

Body mass index and hypogonadism was not significantly associated with a p value of 0.052. There was significant association of BMI and total testosterone with a p value of <0.0001. It is depicted in the figure below. These results suggest that obese subjects were not very symptomatic for hypogonadism even though their total serum testosterone was low.

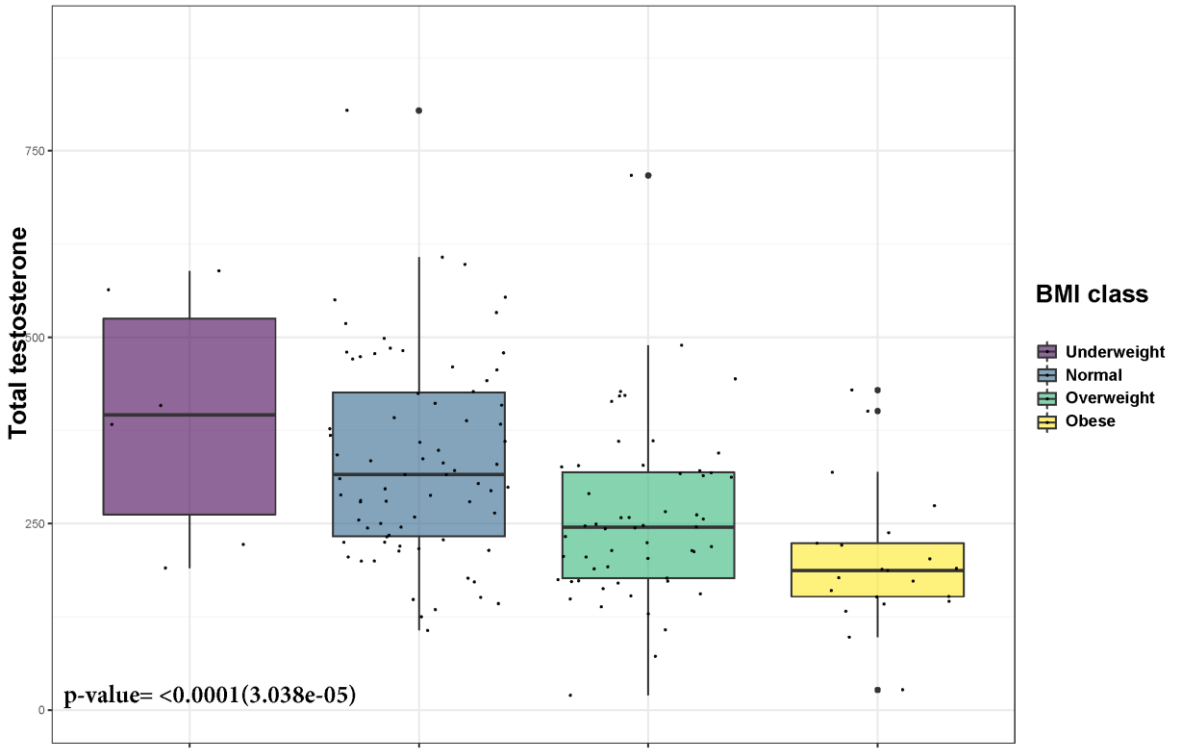


FIGURE 42: ASSOCIATION OF TOTAL TESTOSTERONE WITH BMI

There was however no significant association between BMI and free testosterone (p value 0.083).

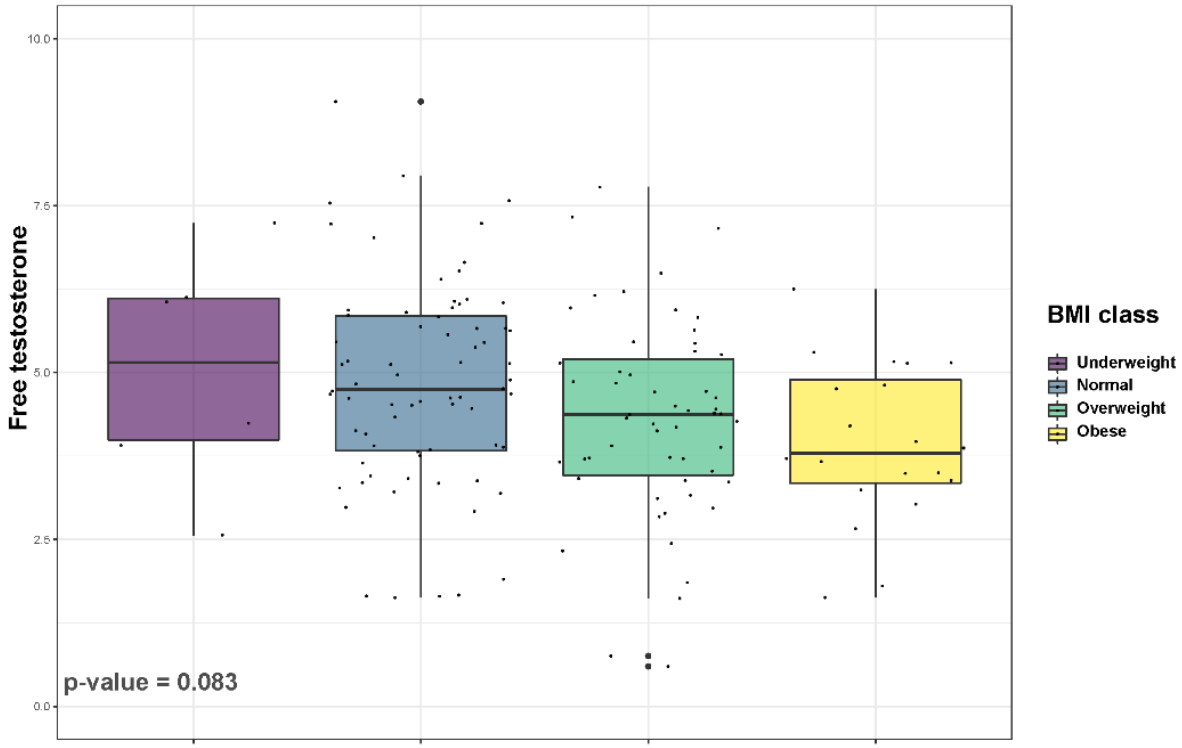


FIGURE 43: ASSOCIATION OF FREE TESTOSTERONE WITH BMI

This difference in significance between free and total testosterone with BMI is because of the decrease in SHBG as BMI increases(p value <0.001). Although the total testosterone was very low in subjects with high BMI, since there was a reduction in SHBG also as BMI increased, the free testosterone was not reduced significantly when BMI increased. However free testosterone also showed a down-ward trend as BMI increased even though it was not statistically significant.

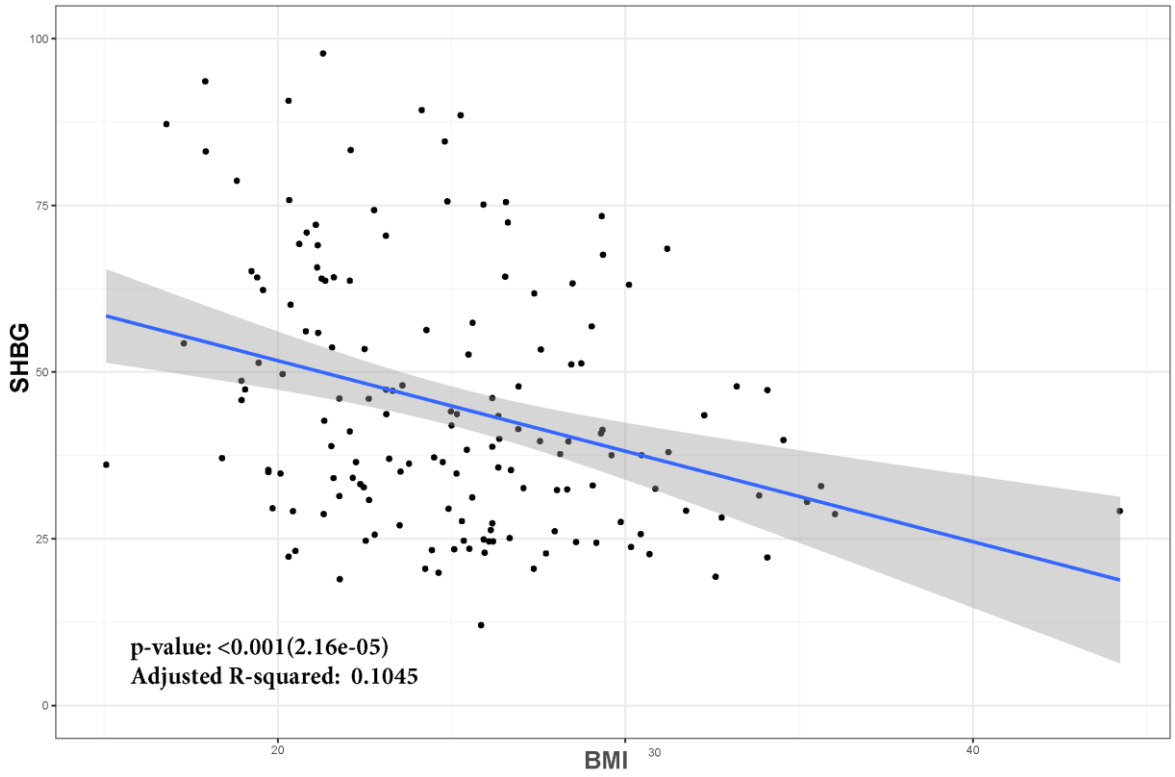


FIGURE 44: ASSOCIATION OF SHBG WITH BMI

HYPOGONADISM AND FRAILTY

There was no significant association between frailty and hypogonadism (p value 0.055) or total serum testosterone (p value 0.075).

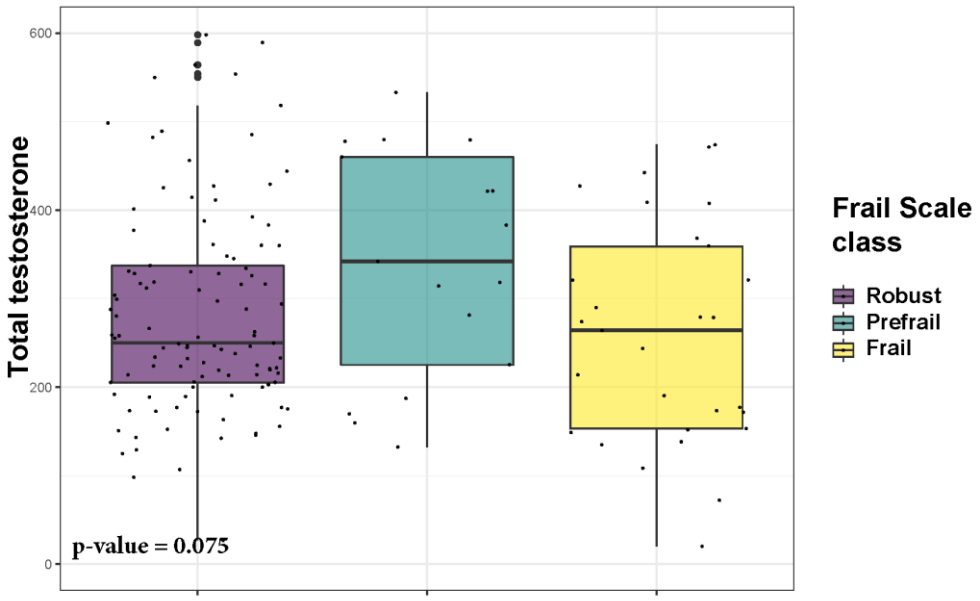


FIGURE 45: ASSOCIATION OF TOTAL TESTOSTERONE WITH FRAILTY

Free testosterone was however significantly associated with frailty(p value 0.0257).

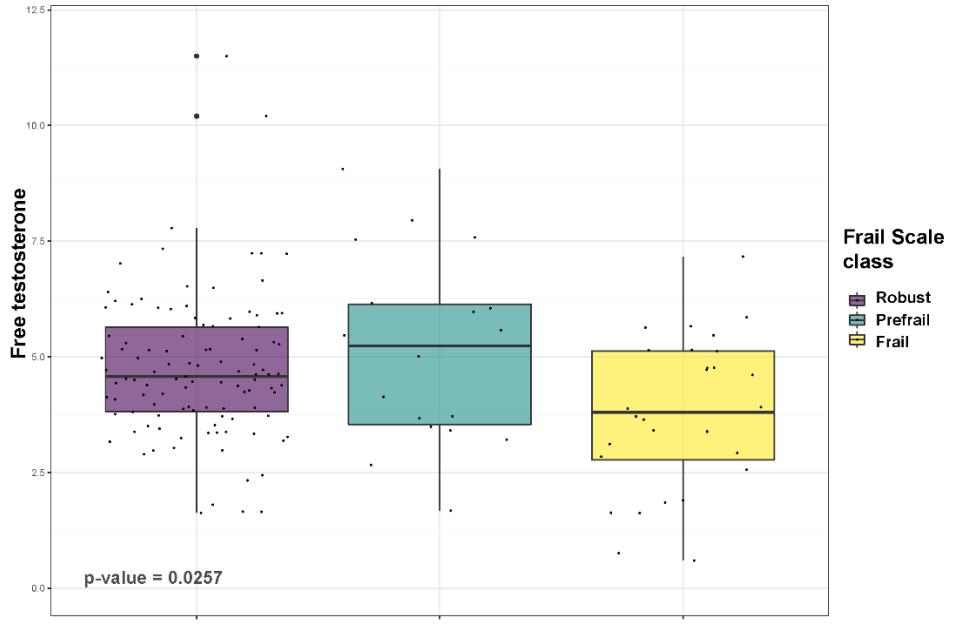


FIGURE 46: ASSOCIATION OF FREE TESTOSTERONE WITH FREE TESTOSTERONE

When subjects were divided into frail/ pre-frail + robust, frailty was significantly associated with hypogonadism. But this significance was not evident when association was checked with free testosterone and total testosterone . When subjects were classified as Robust/frail +pre – frail , there was no significant association found.

TABLE 22: ASSOCIATION OF HYPOGONADISM , TOTAL TESTOSTERONE AND FREE TESTOSTERONE WITH FRAIL + PRE -FRAIL AND ROBUST MEN

	Hypogonadism	Total testosterone	Free testosterone
Frail + Pre-frail	P value 0.023 (OR 2.591, CI 1.117-6.008)	P value 0.396 OR 1.438, CI 0.620-3.333)	P value 0.331 (OR 1.530, CI 0.647-3.618)
Robust	P value 0.276 (OR 0.684, CI 0.345-1.356)	P value 0.380 (OR 1.360, CI 0.684-2.704)	P value 0.810 (OR 1.089, CI 0.543-2.184)

HYPOGONADISM AND ADDICTIONS

There was no significant association with hypogonadism, total testosterone or free testosterone with smoking, alcohol consumption or tobacco chewing.

TABLE 23: HYPOGONADISM AND ADDICTIONS

Addictions	P value	Odds ratio	Confidence interval
Smoking	0.739	1.114	0.590-2.105
Current smoking	0.851		
Alcohol consumption	0.478	1.267	0.659-2.435
Current alcohol consumption	0.657		
Tobacco	0.602	0.805	0.356-1.821

TABLE 24: TOTAL TESTOSTERONE AND ADDICTIONS

Addictions	P value	Odds ratio	Confidence interval
Smoking	0.662	1.156	0.605-2.208
Current smoking	0.785		
Alcohol	0.420	1.316	0.675-2.565
Current alcohol consumption	0.469		
Tobacco	0.980	1.010	0.450-2.270

TABLE 25: FREE TESTOSTERONE AND ADDICTIONS

Addictions	P value	Odds ratio	Confidence interval
Smoking	0.970	1.013	0.528-1.941
Current smoking	0.962		
Alcohol consumption	0.371	1.363	0.691-2.689
Current alcohol consumption	0.354		
Tobacco	0.442	1.391	0.598-3.235

MULTIVARIATE ANALYSIS

On doing multivariate analysis, hypogonadism had a significant association with obesity.

TABLE 26: MULTIVARIATE ANALYSIS - HYPOGONADISM AND VARIOUS FACTORS

Hypogonadism	**P value**	**Odds Ratio**	**95% Confidence Interval**
Diabetes mellitus	0.111	1.756	0.878 - 3.511
Hypertension	0.547	0.718	0.245 - 2.106
Cardiovascular disease	0.331	0.488	0.115 - 2.069
Osteoporosis	0.394	0.593	0.178 - 1.973
Obesity	0.049	4.055	1.006 - 16.337
Frailty	0.069	2.243	0.939 - 5.358
Dyslipidaemia	0.073	1.853	0.945 - 3.636
Ischemic heart disease	0.175	0.376	0.091 - 1.547

Testosterone <300 ng/dL was significantly associated with diabetes and dyslipidaemia.

TABLE 27: MULTIVARIATE ANALYSIS - TOTAL TESTOSTERONE AND VARIOUS FACTORS

Testosterone <300ng/dL	P value	Odds Ratio	95% Confidence Interval
Diabetes Mellitus	0.016	2.332	1.169 - 4.651
Hypertension	0.712	0.815	0.276 - 2.406
Osteoporosis	0.079	0.345	0.105 - 1.131
Cardiovascular disease	0.967	0.972	0.246 - 3.834
Obesity	0.093	3.703	0.802 - 17.093
Frailty	0.517	1.341	0.552 - 3.254
Dyslipidaemia	0.031	2.119	1.070 - 4.199
Ischemic heart disease	0.461	0.614	0.168 - 2.246

Free testosterone <5ng/dL was significantly associated with only cardiovascular disease.

TABLE 28: MULTIVARIATE ANALYSIS -FREE TESTOSTERONE AND VARIOUS FACTORS

Free testosterone < 5 ng/dl	P value	Odds Ratio	95% Confidence Interval
Diabetes	0.233	1.524	0.763 - 3.044
Hypertension	0.746	0.839	0.290 - 2.430
Osteoporosis	0.840	1.122	0.511 - 6.682
Cardiovascular disease	0.045	5.668	1.042 - 30.844
Obesity	0.350	1.982	0.473 - 8.304
Frailty	0.904	1.059	0.421 - 2.663
Dyslipidaemia	0.312	1.430	0.715 - 2.860
Ischemic heart disease	0.626	1.376	0.381 - 4.961

ADAM QUESTIONNAIRE

ADAM questionnaire was administered to all subjects. Since there is no gold standard for diagnosing hypogonadism, the sensitivity and specificity of the ADAM questionnaire for diagnosing a total testosterone value < 300 ng/dl and free testosterone <5 ng/dl was evaluated. To detect total testosterone <300 ng/dl, ADAM questionnaire had a sensitivity of 79.57%(CI 69.95% to 87.23%). However its specificity was very low at 18.18%(CI 9.76% to 29.61%).

TABLE 29:SENSITIVITY AND SPECIFICITY OF THE ADAM QUESTIONNAIRE FOR DIAGNOSING TOTAL TESTOSTERONE VALUE < 300 NG/DL

Statistic	Value	95% CI
Sensitivity	79.57%	69.95% to 87.23%
Specificity	18.18%	9.76% to 29.61%
Positive likelihood ratio	0.97%	0.83 to 1.13
Negative likelihood ratio	1.12	0.59 to 2.15
Positive predictive value	57.81%	54.03% to 61.50%
Negative predictive value	38.71%	24.79% to 54.75%

To detect free testosterone < 5 ng/dl also, ADAM questionnaire had a similar sensitivity and specificity pattern with a sensitivity of 80.41%(CI 71.11%-87.78%) and specificity of 19.35%(10.42% to 87.78%).

TABLE 30: SENSITIVITY AND SPECIFICITY OF THE ADAM QUESTIONNAIRE FOR DIAGNOSING FREE TESTOSTERONE VALUE < 5 NG/DL

Statistic	Value	95% CI
Sensitivity	80.41%	71.11% to 87.78%
Specificity	19.35%	10.42% to 31.37%
Positive likelihood ratio	1.00	0.85 to 1.17
Negative likelihood ratio	1.01	0.53 to 1.94
Positive predictive value	60.94%	57.15% to 64.59%
Negative predictive value	56.60%	48.52% to 64.43%

This results suggest that ADAM score is moderately useful as a screening test. However, it is not very specific and hence there will be large number of false positives.

The specificity and sensitivity of each question in ADAM score to detect total testosterone <300 ng/dl and free testosterone <5 ng/dl was also done

TABLE 31: SENSITIVITY AND SPECIFICITY OF EACH QUESTION OF ADAM QUESTIONNAIRE TO DIAGNOSE TOTAL TESTOSTERONE<300 NG/DL

ADAM score and total testosterone <300 ng /dL

	Sensitivity	**Specificity**
Do you have a decrease in libido(sex drive)?	73.12% (CI 62.93% to 81.79%)	30.30% (CI 19.59% to 42.85%)
Do you have lack of energy?	23.66% (CI 15.46% to 33.60%)	69.7% (CI 57.15% to 80.41%)
Do you have a decrease in strength and/or endurance?	25.81% (CI 17.29% to 35.92%)	72.73% (60.36% to 82.97%)
Have you lost height?	1.08% (CI 0.03% to 5.85 %)	98.48% (CI 91.84% to 99.96%)
Have you noticed a decrease in 'enjoyment of life'	15.05% (CI 8.48% to 23.97%)	72.73% (CI 60.36% to 82.97%)
Are you sad and /or grumpy?	16.13% (CI 9.32% to 25.20%)	72.73% (CI 60.36% to 82.97%)
Are your erections less strong?	75.27% (CI 65.24% to 83.63%)	21.21% (CI 12.11% to 33.02%)
Have you noticed a recent deterioration in your ability to play sports?	24.73% (CI 16.37% to 34.76%)	65.15% (CI 54.42% to 76.47%
Are you falling asleep after dinner?	19.35% (CI 11.89% to 28.85%)	81.82% (CI 70.39% to 90.24%)
Have there been a recent deterioration in your work performance?	26.88% (CI 18.21% to 37.08%)	71.21% (CI 58.75% to 81.70 %)

To detect total testosterone <300 ng/dl, the most sensitive questions were:

1)Do you have a decrease in libido(sex drive)?

2)Are your erections less strong?

The other questions added to the specificity of the test, but were neither very specific nor very sensitive. The question “Are you falling asleep after dinner?” showed a high specificity(81.82%) , but a low sensitivity(19.35%). The significance of this needs to be evaluated further. The question, “Have you lost height?” showed a high specificity(98.48%), but it was not considered very significant as only 2 subjects gave a positive answer to this question.

TABLE 32:SENSITIVITY AND SPECIFICITY OF EACH QUESTION OF ADAM QUESTIONNAIRE TO DIAGNOSE FREE TESTOSTERONE <5 NG/DL

ADAM questionnaire and free testosterone<5 ng/dL		
	Sensitivity	**Specificity**
Do you have a decrease in libido(sex drive)?	75.26% (CI 65.46% to 83.46%)	33.87% (CI 22.33% to 47.01%)
Do you have lack of energy?	24.74% (CI 16.54% to 34.54%)	70.97% (CI 58.05% to 81.80 %)
Do you have a decrease in strength and/or endurance?	25.77% (CI 17.42% to 35.65%)	72. 58% (CI 59.77 % to 83.15%)
Have you lost height?	1.03% (CI 0.03% to 5.61%)	98.39% (CI 91.34% to 99.96 %)
Have you noticed a decrease in ‘enjoyment of life’	17.53% (CI 10.55% to 26.57%)	75.81% (CI 63.26% to 85.78%)
Are you sad and /or grumpy?	18.56% (CI 11.38% to 27.73%)	75.81% (CI 63.26%to 85.78%)
Are your erections less strong?	78.35% (CI 68.83% to 86.07%)	25.81% (CI 15.53% to 38.5 %)
Have you noticed a recent deterioration in your ability to play sports?	26.80% (CI 18.32% to 36.76%)	67.74% (CI 54.66% to 79.06%)
Are you falling asleep after dinner?	14.43% (CI 8.12% to 23.03%)	74.19% (CI 61.50% to 84.47%)
Have there been a recent deterioration in your work performance?	25.77% (CI 17.42% to 35.65%)	69.35% (CI 56.35% to 80.44%)

Similarly, to detect a free testosterone < 5ng/dl also, the questions that were most sensitive were:

1)Do you have a decrease in libido(sex drive)?

2)Are your erections less strong?

The other questions added to the specificity of the questionnaire but were not individually specific or sensitive. Thus instead of administering the full questionnaire, asking at-least these two questions might be useful in a time constrained setting.

DISCUSSION

To the best of our knowledge, this is the first study in India on the prevalence of hypogonadism in those aged 60 and above. Other studies on men above 40 years have been done previously in India. This study also assessed the association between hypogonadism and diabetes mellitus, hypertension, cardiovascular disease, obesity, osteoporosis and frailty which are the commonest comorbidities in elderly.

There is no definite diagnosis of hypogonadism in literature yet. Different guidelines suggest different cut offs and different studies across the world have taken different criteria for diagnosis of hypogonadism. The criteria for hypogonadism in our study was a combination of symptoms of hypogonadism with a total testosterone <300ng/dL. The prevalence of hypogonadism in our study was 47%(n - 74). Total testosterone< 300ng/dL was found in 58% of the participants. When free testosterone <5 ng/dL was considered, the prevalence was even higher at 61%. In a study by Yadav et al in a Delhi hospital, prevalence of hypogonadism, in males aged ≥40 years was 28.99%(14) . Prevalence of men with symptoms of hypogonadism(positive ADAM questionnaire) in the same study was 48.18% while 57.85% had a total testosterone <346ng/dL. A pilot study done by Goel et al. on men in the surgical departments of a hospital in Lucknow found a prevalence of 26.1%(150).

However this study included men between the ages of 40 and 60 only. Besides these were not patients who came to the hospital with any complaints. The HIM study which was conducted on men >/= 45 years visiting the primary care centres in USA showed a prevalence of 38.7%(12). Hypogonadism was defined as those with total testosterone <300ng/dL in this study. Large community studies like the European ageing male study which considered hypogonadism as a combination of symptoms along with a total testosterone <317ng/dL have showed a prevalence of only 2.1% among men aged between 40 and 79. The prevalence of hypogonadism in our study was higher than in any of these studies. The main factor contributing to this disparity is the higher age group of our study population. The community prevalence of hypogonadism is much lower than the prevalence of hypogonadism in men attending a clinic as is evident from the very low prevalence of hypogonadism in the European ageing male study.

The laboratory prevalence of hypogonadism (low total testosterone) was higher than when symptoms were also taken into consideration for diagnosis of hypogonadism . This indicates that the symptoms of hypogonadism does not manifest in all men with total testosterone < 300 ng/dL or free testosterone <5ng/dL. This suggests that a uniform cut off for hypogonadism is difficult to establish. On the contrary, it is pertinent to note that other diseases such as diabetes mellitus and other comorbidities can also manifest with symptoms similar to hypogonadism. This could explain why a large number of patients had normal testosterone levels even though they had symptoms of hypogonadism. Thus it is prudent to check total testosterone or free testosterone to diagnose hypogonadism only in those with definite symptoms.

Our study suggested that age had a significant association with hypogonadism. However total testosterone, though it showed a downward trend, it did not have a significant association with age. However, free testosterone, declined significantly with age. A study conducted by Liu et al. also

showed similar findings where total testosterone was not associated with age but free testosterone was associated with advancing age(11). Another study done by Araujo et al. on the other hand showed a significant association between both total testosterone and free testosterone and age, however free testosterone was more strongly associated with age(13). This marked decline in free testosterone which is out of proportion to the decline in total testosterone is because testosterone binds to SHBG and SHBG levels increases with aging.(17). Our study showed a steady increase in SHBG as age increased and a dramatic increase in SHBG after the age of 75. Other parameters like bioavailable testosterone and free testosterone index also followed a similar pattern to free testosterone.

ADAM questionnaire was used as a screening tool for symptoms of hypogonadism in our study. We found a sensitivity of 79.57% to detect total testosterone <300ng/dL and 80.41% to detect a free testosterone of <5ng/dL. Various studies conducted globally have found a sensitivity ranging from 83.3–97%(41).The specificity of the questionnaire was 18.18% to detect a total testosterone<300ng/dL and 19.35% to detect a free testosterone <5ng/dL in our study. The specificity of the ADAM questionnaire from studies conducted all over the world also ranges between 19.7–36.6%(41). ADAM questionnaire is widely used as a screening tool for hypogonadism, but while it is moderately sensitive, its specificity is very poor. The questions , ‘ Do you have decreased libido?’ and “Are your erections less strong’ individually had the maximum sensitivity. These 2 questions can be used in a busy clinic setting as an easy screening method for suspecting hypogonadism. However, caution needs to be exercised of false negative answers as the sensitivity is low.

The association of comorbidities commonly seen in elderly patients with hypogonadism was also assessed in our study. Diabetes had a significant association with hypogonadism and total

testosterone both on univariate and multivariate analysis, but was not significantly associated with free testosterone level.. Many studies have shown an inverse bidirectional relationship between diabetes and hypogonadism(61),(60),(58), (62). Studies have shown that SHBG is low in those with diabetes mellitus(151). However, most studies show a decrease in free testosterone as well in diabetic patients.. But the low SHBG in diabetic could explain why in our study there was no significant association between free testosterone and diabetes mellitus.

We found a significant association between BMI and total testosterone in our study. On multivariate analysis, we found BMI had a significant association with hypogonadism (symptoms + total testosterone <300 ng/dL).. Large community studies like the European male ageing study and the Massachusetts Male Ageing Study have revealed a significantly lower total testosterone and free testosterone in obese men.(118). (120).(119).A decline in SHBG was noticed with increase in in BMI in our study. This association was seen in most other studies in different populations(121). This probably explains why free testosterone levels did not correlate with BMI even when total testosterone decreased down significantly with BMI.

Frailty had a significant association with free testosterone but not with total testosterone or hypogonadism in our study. The association between frailty and hypogonadism is moderate in studies done across the world. A study done by Roy et al. showed that muscle strength was significantly associated with free testosterone and not with total testosterone(92). This is consistent with our results also. Another study done by Mohr et al. did not show any significant association of testosterone or free testosterone with frailty, but SHBG had a significant association with frailty(91). It is known that SHBG is high in frail men(152). This explains why free testosterone may be disproportionately lower in frail men when compared to total testosterone.

Cardiovascular disease did not have any significant association with hypogonadism, as well as total or free testosterone. On multivariate analysis, however cardiovascular disease had a significant association with free testosterone. Cardiac disease had a significant association with free testosterone, though not with hypogonadism and total testosterone. Many Indian (153) (154)and global studies(73) done suggested testosterone can be a predictor of severity of coronary artery disease. The diagnosis of cardiovascular disease in our study was limited by the fact that neither angiography was performed nor was brain imaging done to look for cerebrovascular disease in our subjects. Diagnosis of cardiovascular disease was primarily based on ECG findings and previous history of cardiovascular disease.

We found that the prevalence of osteoporosis was low in those with low testosterone in our study. This contradictory result was thought to be due to the effect BMI had on osteoporosis and total testosterone. Osteoporosis was less prevalent and total testosterone as well was lower in obese individuals. Multivariate analysis done however showed osteoporosis had no association with hypogonadism, total testosterone or free testosterone. Association between osteoporosis and hypogonadism has been inconsistent in published studies.. A meta-analysis done by Liu et al. did not show any significant association between testosterone levels and osteoporosis(110).

Hypertension was not associated with hypogonadism, total testosterone or free testosterone. Use of ACE inhibitors and calcium channel blockers had a significant association with total testosterone. A study done by Koshida et al showed lisinopril reduced total testosterone in hypertensive men(155) . Various animal studies also have shown a reduction in total testosterone levels by calcium channel blockers(156). Further studies are needed to evaluate the effect of various antihypertensives on testosterone levels.

Our study showed that dyslipidaemia had a significant association with hypogonadism and total testosterone. This association was significant even on multivariate analysis.

Other factors like smoking and alcohol consumption did not have any significant association with hypogonadism , total testosterone or free testosterone.

Table 33 summarises our results (numbers denote p values)

TABLE 33: SUMMARY OF RESULTS

Comorbidities	Hypogonadism	Total testosterone	Free testosterone
Age	0.035	0.3742	0.0034
Diabetes	0.025	0.012	0.052
Body Mass Index	0.052	<0.001	0.083
Frailty	0.055	0.075	0.0257
Dyslipidaemia	0.016	0.005	0.209
Osteoporosis	0.373	0.017	0.943
Ischemic Heart Disease	0.912	0.171	0.009
Cardiovascular disease	0.232	0.072	0.136
Hypertension	0.461	0.077	0.127

LIMITATIONS

1. We did not reach sample size because of the ongoing COVID 19 pandemic.
2. Free testosterone was derived using a calculator with values of SHBG, albumin and total testosterone
3. In this study, we did testosterone only once while the recommendations suggest to do it twice for the diagnosis of hypogonadism.
4. The study was hospital based. Hence, it may not be possible to extrapolate these findings to community dwelling older adults.

CONCLUSIONS

1. The prevalence of hypogonadism(Men with symptoms of hypogonadism along with total testosterone < 300 ng/dl) in our study was 47%(n - 74)

2. Total testosterone< 300ng/dl was prevalent in 58% and free testosterone <5 ng/dl was prevalent in 61%.
3. Age, diabetes, obesity and dyslipidaemia had a significant association with hypogonadism(symptoms + testosterone < 300 ng/dl) in our study.
4. Diabetes, BMI and dyslipidaemia had a significant inverse association with total testosterone.
5. Free testosterone had a significant association with age, cardiovascular disease, ischemic heart disease and frailty.
6. Adams questionnaire had a sensitivity of 79.57% and specificity of 18.18 % to detect total testosterone less than 300 ng/dl. Its sensitivity and specificity to detect free testosterone < 5 ng/dl was slightly higher at 80.41% and 19.35% respectively.

FUTURE DIRECTIONS

The prevalence of hypogonadism is quite high in men above 60 years. It is also associated with many of the comorbid conditions prevalent in men above 60 years. Clinicians should think of the possibility of underlying hypogonadism in men especially in those with multiple comorbidities. There is still controversy regarding giving testosterone replacement therapy in elderly men with hypogonadism. Further studies are required. Clinicians can however consider testosterone replacement therapy if symptoms are significant and there are no contraindications in these men. The absence of a clear cut off for total testosterone is also a major disadvantage and more community studies are required for more precise estimations of hypogonadism. What testosterone cut off is a significant risk for various comorbidities associated with hypogonadism also needs to be assessed. Large, multicentric studies in different find racial and ethnic differences in testosterone values also needs to be performed.

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APPENDIX

1. INSTITUTIONAL REVIEW BOARD APPROVAL LETTER

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. **B.J. Prashantham,** M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

June 06, 2019

Dr. Raeba Eldhose,
PG Registrar,
Department of Geriatric Medicine,
Christian Medical College,

Sub: **Fluid Research Grant: New Proposal:**
The Prevalence of hypogonadism and its association with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis, frailty and obesity in elderly men attending geriatric OPD at a tertiary care center in South India
Dr. Raeba Eldhose, PG registrar, Department of Geriatric Medicine, Dr. K.G. Gopinath, Department of Geriatric Medicine, Dr. Joseph Dian Bondu, Clinical Biochemistry, Ms. K. Reka, Biostatistics.

Ref: IRB Min. No. 11704 [OBSERVE] dated 05.12.2018

Dear Dr. Raeba Eldhose,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Biju George, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

CC: Dr. K.G. Gopinath, Geriatric Medicine, CMC, Vellore

1 of 5

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. **Prashantham,** M.A., M.A., Dr Min (Clinical)
Director, Christian Counseling Center,
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June 06, 2019

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Dr. Raeba Eldhose, PG registrar, Department of Geriatric Medicine, Dr. K.G. Gopinath, Department of Geriatric Medicine, Dr. Joseph Dian Bondu, Clinical Biochemistry, Ms. K. Reka, Biostatistics.

Ref: IRB Min. No. 11704 [OBSERVE] dated 05.12.2018

Dear Dr. Raeba Eldhose,

The Institutional Review Board (**Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "The Prevalence of hypogonadism and its association with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis, frailty and obesity in elderly men attending geriatric OPD at a tertiary care center in South India." On December 03rd 2018.

The Committee reviewed the following documents:

1. IRB application format
2. Patient Information Sheet and Consent Form (English, Tamil, Hindi)
3. Proforma
4. Cvs of Drs. Gopinath, Joseph, Ms. Reka.
5. No. of documents 1- 4

The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on December 03rd 2018 in the New IRB Room, Bagayam, Christian Medical College, Vellore 632 004.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Dr. **B.J. Prashantham,** M.A., M.A., Dr. Min (Clinical)
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Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Name	Qualification	Designation	Affiliation
Dr. Biju George	MBBS, MD, DM	Professor, Haematology, Research), Additional Vice Principal , Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. B. J. Prashantham	MA(Counseling Psychology), MA(Theology), Dr. Min(Clinical Counselling)	Chairperson, Ethics Committee, IRB. Director, Christian Counseling Centre, Vellore	External, Social Scientist
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Dr. Ratna Prabha	MBBS, MD (Pharma)	Associate Professor, Clinical Pharmacology, CMC, Vellore	Internal, Pharmacologist
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert
Dr. John Jude Prakash	MBBS, MD,	Professor, Clinical Virology, CMC, Vellore	Internal, Clinician
Dr. Rekha Pai	BSc, MSc, PhD	Associate Professor, Pathology, CMC, Vellore	Internal, Basic Medical Scientist
Mrs. Sophia V	M.Sc Nursing	Addl. Deputy Dean CMC, Vellore	Internal, Nurse
Dr. Ekta Rai	MBBS, MD MRCA	Professor, Department of Anaesthesia, CMC, Vellore	Internal, Clinician
Rev. Joseph Devaraj	BSc, BD	Chaplaincy Department, CMC, Veljore	Internal, Social Scientist
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC, Vellore	Internal, Clinician
Dr. Jayaprakash Muliyil	BSC, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist & Epidemiologist

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Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Mrs. Nirmala Margaret	MSc Nursing	Addl. Deputy Nursing Superintendent, College of Nursing, CMC, Vellore	Internal, Nurse
Dr. Asha Solomon	MSc Nursing	Associate Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Santhanam Sridhar	MBBS, DCH, DNB	Professor, Neonatology, CMC, Vellore	Internal, Clinician
Dr. Ajith Sivadasan	MD, DM	Professor, Neurological Sciences, CMC, Vellore	Internal, Clinician
Mrs. Sheela Durai	MSc Nursing	Professor, Medical Surgical Nursing, CMC, Vellore	Internal, Nurse
Dr. Winsely Rose	MBBS, MD (Paed)	Professor, Paediatrics, CMC Vellore	Internal, Clinician
Dr. Premila Abraham	M.Sc. Ph.D	Professor, Department of Biochemistry, CMC, Vellore	MBBS, MD (Paed)
Dr. Shyam Kumar NK	MBBS, DMRD, DNB, FRCR, FRANZCR	Professor, Radiology, CMC, Vellore	Internal, Clinician
Dr. Vivek Mathew	MD (Gen. Med.) DM (Neuro) Dip. NB (Neuro)	Professor, Neurology, CMC, Vellore	Internal, Clinician
Ms. Grace Rebekah	M.Sc., (Biostatistics)	Lecturer, Biostatistics, CMC, Vellore	Internal, Statistician
Dr. Barney Isaac	MBBS, DNB (Respiratory Diseases)	Associate Professor, Pulmonary Medicine, CMC, Vellore	Internal, Clinician

We approve the project to be conducted as presented.

Kindly provide the total number of patients enrolled in your study and the total number of Withdrawals for the study entitled: "The Prevalence of hypogonadism and its association with diabetes mellitus, hypertension, cardiovascular disease, osteoporosis, frailty and obesity in elderly men attending geriatric OPD at a tertiary care center in South India" On a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in).

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Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Fluid Grant Allocation:

A sum of 1,00,000/- INR (Rupees One Lakh Only) will be granted for 24 Months.

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board

Dr. BIJU GEORGE
MBBS., MD., DM.
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board
Christian Medical College, Vellore - 632 002.

IRB Min. No. 11704 [OBSERVE] dated 03.12.2018

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2. PATIENT INFORMATION SHEET

ENGLISH

Patient information sheet

Study title : The Prevalence of hypogonadism and it's association with diabetes, hypertension, cardiovascular disease, osteoporosis, frailty and obesity in elderly men attending geriatric OPD at a tertiary care center in South India.

What is this study about ?

Testosterone is the hormone present in males responsible for characteristic features of male body. Some people have a low level of testosterone in their body from younger age and some develop it later in life. Low level of testosterone in their body is called hypogonadism. We would like to find out the percentage of people who have hypogonadism. We would also like to see whether it is associated with high percentage of diabetes mellitus, hypertension, heart diseases, stroke, obesity or bone mineral density.

What will happen if you participate in this study?

If you agree to participate in this study, you will have to attend an interview by a doctor and answer questions pertaining to your comorbidities, previous surgeries, treatment history and sexual history. A detailed physical examination will be done on you which will include your blood pressure examination also. You will be required to give blood samples for tests pertaining to the study along with your routine blood tests. You will also be required to do a DEXA scan, which is similar to an x-ray.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

As this is an observational study which does not involve any new treatment methods or interventions, you are not expected to develop any new treatment related injury. Blood tests will be done along with your routine tests. DEXA scans use a much lower level of radiation than standard X-ray examinations. The amount of radiation used during a DEXA scan is very low and less than two days' exposure to natural background radiation (NBR).

Will you have to pay for the tests?
A few blood tests and a DEXA scan will be done for the purpose of the study. All the tests done for the purpose of the study, which are not a part of your routine tests will be free of cost.

What happens after the study is over?
When the entire study is completed the findings will be analysed and the results will be published in a scientific journal for other doctors to understand and better help their patients.

Will your personal details be kept confidential?
Confidentiality will be maintained at all times. Your identity will not be revealed at any point of time to a third party. The results of this study will be published in a medical journal but

you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr.Raeba Eldhose(9894609152), Dr. K.G. Gopinath (9600915737) or email: raebaeldhose@gmail.com

TAMIL

CHRISTIAN MEDICAL COLLEGE, VELLORE

DEPARTNMENT OF GERIATRICS

தகவல் தாள்

முதியோர் மருத்துவ பிரிவு

மூன்றாம் நிலை மருத்துவமனை, முதியோர் மருத்துவ பிரிவு, புறநோயாளிகளின் பிரிவில் Hypogonadism -த்தின் நோய்த்தாக்கம் மற்றும் அதனுடன் தொடர்புடைய சர்க்கரை வியாதி, உயர் இரத்த அழுத்தம், இருதய சம்பந்தப்பட்ட நோய், எலும்பு தேய்மானம், பலவீனம் மற்றும் உடல் பருமன் கொண்ட ஆண் முதியவர்களை பற்றிய ஆய்வு:

ஆய்வு பற்றி:

டெஸ்டோஸ்டிரோன் என்பது ஆண் உடலில் உள்ள ஒரு ஹார்மோன் ஆகும். இந்த ஹார்மோனின் அளவு சில ஆண்களில் உடலில் சிறு வயது முதலே குறைவாக இருக்கும். சிலரின் உடலில் வயது ஆக ஆக குறையும். உடலில் டெஸ்டோஸ்டிரோன் குறைந்த அளவில் ர்ன்ழபழபெனஅனை அ என்று அழைக்கப்படுகிறது. Hypogonadism உள்ள ஆண்களின் சதவீதம் அறிய விரும்புகிறோம். Hypogonadism மற்றும் அதனுடன் தொடர்புடைய சர்க்கரை நோய், உயர் இரத்த அழுத்தம், இருதயம் சம்பந்தப்பட்ட நோய், எலும்பு தேய்மானம், பலவீனம் மற்றும் உடல் பருமன் போன்ற பிரச்சனைகளை பற்றி அறிய விரும்புகிறோம்.

இந்த ஆய்வில் பங்கேற்பதால் ஏற்படும் விளைவு:-

இந்த ஆய்வில் பங்கேற்பதால், உங்களுக்கு ஒரு நேர்காணல் நடத்தப்படும். உங்களின் முந்தைய மருத்துவ விவரங்கள் மற்றும் அறுவைச்சிகிச்சை தொடர்பான கேள்விகளுக்கு விடையளிக்க வேண்டும். பிறகு உங்களுக்கு முழு உடல் பரிசோதனை செய்யப்படும். உங்களுடைய வழக்கமான பரிசோதனைகளுடன் சில இரத்த பரிசோதனைகள் மற்றும் X-Ray செய்ய வேண்டி வரும்.

ஆய்வு தொடங்கிய பிறகு விலக முடியுமா?

இவ்வாய்வு முழுமையும் உங்கள் விருப்பம் சார்ந்தது. இவ்வாய்வின் பங்கேற்பிலிருந்து விலகுவதற்கும் உங்களுக்கு உரிமை உண்டு. உங்களின் மறுப்பு அல்லது விலகுதல் சிகிச்சையின் தரத்தினை பாதிக்காது.

ஆய்வு தொடர்பான காயம் ஏற்பட்டால் என்ன நடக்கும்?

இது கண்காணிப்பு ஆய்வு என்பதாலும், இதில் எந்த புதிய சிகிச்சை முறைகள் உள்ளடக்கவில்லை என்பதாலும், ஆய்வு தொடர்பான காயம் ஏற்பட வாய்ப்பு இல்லை.

நீங்கள் பரிசோதனைகளுக்கு கட்டணம் செலுத்த வேண்டுமா?

உங்களுடைய வழக்கமான பரிசோதனைகளை தவிர இந்த ஆய்விற்கு உட்பட்ட பரிசோதனைகள் உங்களுக்கு இலவசமாக செய்யப்படும்.

ஆய்வு முடிந்த பின்னர் என்ன நடக்கும்?

முழு ஆய்வு முடிந்த பிறகு கண்டுபிடிப்புகள் ஆய்வு செய்யப்பட்டு மற்று மருத்துவர்கள் புரிந்துகொள்ள மற்றும் தங்கள் நோயாளிகளுக்கு சிறந்த சிகிச்சை கொடுக்க ஆய்வின் முடிவுகள் அறிவியல் பத்திரிக்கையில் வெளியிடப்படும்.

உங்களுடைய சுய விவரங்கள் இரகசியமாக வைக்கப்படுமா?

இந்த ஆய்வின் முடிவுகள் மருத்துவ இதழில் வெளியிப்படலாம். ஆனால் முடிவுகளிலுடைய எந்த வெளியீட்டிலும் அல்லது எடுத்துரைத்தலிலும் உங்கள் பெயர் குறிப்பிடப்பட மாட்டாது. எனினும், உங்கள் மருத்துவ குறிப்புகள் உங்கள் கூடுதல் அனுமதி இல்லாமல், ஆய்வு தொடர்புடைய மக்களால் மதிப்பாய்வு செய்யப்படலாம்.

ஏதேனும் வினாக்கள் இருப்பின் தொடர்பு கொள்ள வேண்டியது நபர்:

டாக்டர். ரேபா எல்டோஸ் (0207449652)

தொலைபேசி: 0416-2282943

மின்னஞ்சல் முகவரி: raebaeldhose@gmail.com

HINDI

CHRISTIAN MEDICAL COLLEGE , VELLORE

DEPARTMENT OF GERIATRICS

रोगी सूचना पत्र

अध्ययन शीर्षक

हाइपोगोनाडिज्म (प्रजनन ग्रंथिरस की कमी) का प्रसार तथा इसका वृद्ध पुरुषों में उच्च रक्तचाप, मधुमेह, हृदय रोग, मोटापा तथा आस्टियोपोरोसिस (हड्डियों की कमजोरी) से संबंध जो दक्षिण भारत के एक त्रितकीय अस्पताल में इलाज के लिए बाह्य रोगी विभाग में आते है।

यह अध्ययन किस बारे में है?

टेस्टोस्टेरॉन पुरुषों में एक हार्मोन (ग्रंथिरस) होता है जो कि उनकी विशेष शारीरिक संरचना के लिए आवश्यक होता है। कुछ लोगों में टेस्टोस्टेरॉन की कमी बचपन से तथा कुछ लोगों में वृद्धावस्था के कारण हो सकती है। शरीर में टेस्टोस्टेरॉन की कमी को हाइपोगोनाडिज्म कहते हैं। इस अध्ययन में हम यह देखेंगे कि क्या हाइपोगोनाडिज्म का संबंध अधिक मात्रा में मधुमेह, उच्च रक्तचाप, लकवा, मोटापा, हृदय रोग, तथा आस्टियोपोरोसिस से है या नहीं।

आपके इस अध्ययन में भाग लेने से क्या होगा?

यदि आप इस अध्ययन में भाग लेने की सहमति देते हैं तो आपका एक चिकित्सक द्वारा साक्षात्कार किया जाएगा तथा आपके अन्य रोगों के विषय में, आपकी पहले की शल्य चिकित्सा तथा आपके यौन जीवन के विषय में प्रश्न किए जाएंगे। आपके रक्तचाप की जांच तथा अन्य रक्त परीक्षण भी किए जाएंगे। आपका डेक्सा स्केन भी किया जाएगा जो कि एक एक्स रे जैसी प्रक्रिया होती है।

क्या आपको इस अध्ययन से कोई शारीरिक हानि होगी?

क्योंकि यह एक अवलोकन अध्ययन है जिसमें किसी भी नई जांच प्रणाली का इस्तेमाल नहीं किया जाएगा, इसलिए इस अध्ययन में आपको कोई शारीरिक हानि नहीं होगी।

क्या इस अध्ययन में भाग लेने से आपको कोई अतिरिक्त खर्च लगेगा?

सामान्य रक्त जाँच तथा डेक्सा स्केन इस अध्ययन के लिए किए जाएंगे। इसके अतिरिक्त कोई भी जांच मुफ्त में की जाएगी।

अध्ययन समाप्त होने के बाद क्या होगा?

अध्ययन समाप्त होने के बाद इसके परिणामों का विश्लेषण एक वैज्ञानिक पत्रिका में प्रकाशित किया जाएगा।

क्या आपकी निजी जानकारी गुप्त रखी जाएगी?

आपकी निजी जानकारी की गोपनीयता का ध्यान रखा जाएगा। जिस वैज्ञानिक पत्रिका में यह प्रकाशित होगा उसमें आपका नाम गुप्त रखा जाएगा। किंतु आपके चिकित्सकीय अभिलेखों को इस अध्ययन से जुड़े लोगों द्वारा देखा जा सकेगा और इसके लिए आपकी अतिरिक्त अनुमति नहीं ली जाएगी।

यदि आपके अन्य प्रश्न है तो आप निम्नलिखित दूरभाष क्रमांक अथवा ई मेल पर संपर्क कर सकते है।

डॉ रेबा एतदोस - 9894609152

डॉ के जी गोपीनाथ - 9600915737

ई मेल - [redacted]

3. CONSENT FORMS

ENGLISH

1. **Study Title** The Prevalence of hypogonadism and it's association with diabetes, hypertension, cardiovascular disease, osteoporosis, frailty and obesity in elderly men attending geriatric OPD at a tertiary care center in South India

Informed Consent form to participate in a research study
Study Number: _____
Subject's Initials: _____ **Subject's Name:**
_____
Hospital Number: _____
Date of Birth / Age: _____
Address and Phone Number: _____
_____
Phone:_____
(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable
Date: _____/_____/_____

Signatory's Name: _____ :

Signature of the Investigator: _____
Date: _____/_____/_____
Study Investigator's Name:Dr.Raeba Eldhose
Contact details of the study investigator : 9894609152

Signature or thumb impression of the Witness: _____
Date: _____/_____/_____
Name & Address of the Witness: _____

TAMIL

CHRISTIAN MEDICAL COLLEGE, VELLORE
DEPARTNMENT OF GERIATRICS

மூன்றாம் நிலை மருத்துவமனை முதியோர் மருத்துவ பிரிவு, புற நோயாளிகளின் பிரிவில் Hypogonadism-த்தின் நோய்தாக்கம் மற்றும் அதனுடன் தொடர்புடைய சக்கரை வியாதி, உயர் இரத்த அழுத்தம், இருதயம் சம்பந்தப்பட்ட நோய், எலும்பு தேய்மானம், பலவீனம் மற்றும் உடல் பருமன் கொண்ட ஆண் முதியவர்களை பற்றிய ஆய்வு.

ஆய்வு எண் : .....

நோயாளியின் பெயர் : .....

பிறந்த தேதி / வயது : .....

பொருள்:

1) நான் மேற்கண்ட ஆய்வுக்காக ..... தேதியிட்ட தகவல் தாள் படித்து புரிந்து கொண்டேன் என்பதை உறுதிபடுத்துகிறேன். மற்றும் கேள்விகளை கேட்க வாய்ப்பு கிடைத்துள்ளது.
2) இந்த ஆய்வில் பங்கேற்பது தன்னார்வமாக உள்ளது. நான் எந்த நேரத்திலும் எந்தவொரு காரணமும் இல்லாமல், எனது மருத்துவ கவனிப்பு அல்லது சட்ட உரிமைகள் பாதிக்கப்படாமல் இந்த ஆய்வினிருந்து விலகலாம் என்பதை நான் புரிந்துகொள்கிறேன்.
3) நடப்பு ஆய்வு மற்றும் அதைப்பற்றிக் கலந்துரையாடக்கூடிய எந்தவொரு ஆராய்ச்சிக்கும் பொருந்திய எனது சுகாதார பதிவேடுகளைப் பார்க்க நெறிமுறைக் குழுவும் ஒழுங்குமுறை நான் புரிந்து கொள்கிறேன். சோதனை இந்த அனுகலை நான் ஏற்கிறேன். என்னுடைய மருத்துவ பதிவேடுகள் மூன்றாம் தரப்பினருக்கு வழங்கவோ, எந்த தகவலிலும் வெளியிடவோ முடியாது என்று நான் புரிந்து கொள்கிறேன்.
4) என்னுடைய மருத்துவ பதிவேடுகள் மற்றும் ஆய்வின் முடிவுகள் அனைத்தும் விஞ்ஞான நோக்கங்களுக்கு மட்டுமே பயன்படுத்தப்படுகிறது என்பதை புரிந்து கொள்கிறேன்.
5) மேலேயுள்ள ஆய்வில் பங்கேற்க நான் ஒப்புக்கொள்கிறேன்.

நோயாளி / சட்டப்பூர்வமாக ஏற்றுக்கொள்ளப்பட்ட கையொப்பம் (அல்லது கைவிரல் ரேகை)

தேதி : .....

கையொப்பமிட்ட பெயர் : .....

கையொப்பம் : .....

அல்லது

பிரதிநிதி : .....

தேதி : .....

கையொப்பமிட்ட பெயர் : .....

ஆராய்ச்சியாளரின் கையொப்பம் : .....

தேதி : .....

ஆய்வு ஆராய்ச்சியாளரின் பெயர் : .....

சாட்சியின் கையொப்பம் அல்லது கை ரேகை :

.....

தேதி : .....

சாட்சியின் பெயர் மற்றும் முகவரி : .....

HINDI

CONSENT FORM

अध्ययन शीर्षक

हाइपोगोनाडिज्म (प्रजनन ग्रंथिरस की कमी) का प्रसार तथा इसका वृद्ध पुरुषों में उच्च रक्तचाप, मधुमेह, हृदय रोग, मोटापा तथा आस्टियोपोरोसिस (हड्डियों की कमजोरी) से संबंध जो दक्षिण भारत के एक त्रितकीय अस्पताल में इलाज के लिए बाह्य रोगी विभाग में आते हैं।

सूचित सहमति पत्र

नाम

जन्म तिथि /उम्र

पता

दूरभाष क्रमांक

अध्ययन संख्या

हास्पिटल क्रमांक

1. मैं इस बात की पुष्टि करता/करती हूं कि मुझे दिये गये सूचना पत्र को मैंने ध्यान से पढा और समझा है तथा इस पर सवाल पूछने का अवसर भी मुझे मिला है।

2. मैं समझता /समझती हूं कि मेरा/मेरे रिश्तेदार का इस अभ्यास में भाग लेना स्वैच्छिक है तथा मुझे /मेरे रिश्तेदार को बिना कोई कारण दिए इस अभ्यास से निकलने की आजादी होगी जिसका असर मेरी चिकित्सा अथवा कानूनी अधिकारों पर नहीं पड़ेगा।

3. मैं समझता /समझती हूं कि आचार समिति तथा नियामक अधिकारी को बिना मेरी /मेरे रिश्तेदार की अतिरिक्त अनुमति के चिकित्सा अभिलेखों को देखने का अधिकार होगा इसके बावजूद कि मैं /मेरे रिश्तेदार इस अध्ययन से अपना नाम वापस ले लेते हैं। हालांकि मेरे /मेरे रिश्तेदार की पहचान किसी तीसरे पक्ष के सामने या किसी प्रकाशन में जारी नहीं की जाएगी।

4. मैं इस बात से सहमत हूँ कि मैं इस अध्ययन के आधार सामग्री अथवा परिणामों के उपयोग को प्रतिबंधित नहीं करूंगा /करूंगी यदि उसका इस्तेमाल वैज्ञानिक उद्देश्य के लिए हो।

5. मैं इस अध्ययन में भाग लेने की सहमति देता /देती हूं।

हस्ताक्षर /अंगूठे के निशान

तारीख

हस्ताक्षर करने वाले का नाम

मरीज से संबंध

अन्वेषक के हस्ताक्षर

तारीख

अन्वेषक का नाम

साक्षी के हस्ताक्षर /अंगूठे के निशान

तारीख

साक्षी का नाम और पता

4. PROFORMA

Name		
Age		
Hospital no.		
State		
Phone number		
Email id		
Education		
	<5	
	6-12	
	Diploma	
	Masters	
Occupation	Present	
	Previous	
Income		
SES		
LIVING WITH		
Living in		

Exclusion criteria	
Hypopituitarism	
Renal failure	
Liver cirrhosis	
Malignancy	
Autonomic neuropathy	

Testosterone replacement therapy	
Hormones	
Anti-Androgens	
Androgens	
Antifungal agents	
Steroid agents	
Prostate surgery	
BPH treatment	

Serum testosterone		
Free testosterone index		
Diabetes		
	Ac	
	Pc	
	Hba1c	
	Random glucose	
	Duration	
	Oha	
	Insulin	
Hypertension	Bp	
	Duration	
	Medications	

Cardiovascular disease	ECG changes	
	Past history of mi	
	CABG history	
	Stroke in the past	
Osteoporosis	T score <2.5	
	Z score <2.5	
Obesity	Weight	
	Height	
	BMI	

Comorbidities		

Smoking	Yes	No
	Duration	
Alcohol	Yes	No
	Duration	
Other addictions		

ADAM QUESTIONNAIRE

Sl	Questionnaires	Comments
1	Do you have a decrease in libido (sex drive)?	Yes / No
2	Do you have a lack of energy?	Yes / No
3	Do you have a decrease in strength and/or and endurance?	Yes / No
4	Have you lost height?	Yes / No
5	Have you noticed a decreased 'enjoyment of life'?	Yes / No
6	Are you sad and/or grumpy?	Yes / No
7	Are your erections less strong?	Yes / No
8	Have you noticed a recent deterioration in your ability to play sports?	Yes / No
9	Are you falling asleep after dinner?	Yes / No
10	Has there been a recent deterioration in your work performance?	Yes / No

Test is considered positive if answers are 'Yes' to question 1, question 7, or any 3 other questions.

	FRAILTY INDEX		Score
Weight loss >5% in the last 1 year			1
Exhaustion			1
Slow walking speed(>6-7 sec to walk 15 feet)			1
If 3 are positive / if 3 are negative, do not need to perform next 2			
Weakness (decreased grip strength)			1
Decreased physical activity (Short physical performance battery)	Stand and sit Time Stop when using hand/finished 5/after 1 minute if not completed 5	Time	
		>16.7 sec. - 1	
		13.7 – 16.69 - 2	
		11.2 – 13.69- 3	
		<11.19. -4	
	Standing -10 sec 1. Feet together	Yes -1	
		No -0	
	Semi tandem	Yes - 1	
		No -0	
	Full tandem	Yes - 2	

		3-10 sec - 1	
		No -0	
	3 m walk test	>6.52 sec - 1	
		4.66 sec – 6.52 sec - 2	
		3.62 -4.65 sec -3	
		<3.62 sec - 4	
	Total score		
		>10	
		<10	

FRAIL SCALE		
1.	"Have you felt fatigued? Most or all of the time over the past month?"	Yes No
2.	"Do you have difficulty walking one block?"	Yes No
3.	"Do you have difficulty walking one block?"	Yes No
4.	“Do you have any of these illnesses: hypertension, diabetes, cancer (other than a minor skin cancer), chronic lung disease, heart attack, congestive heart failure, angina, asthma, arthritis, stroke, and kidney disease?”) Five or greater = 1	Yes No
5.	“Have you lost more than 5 percent of your weight in the past year?”	Yes No

Frail – scores 3 to 5

Pre-frail - 1 to 2

Robust – 0

5. HYPOGONADISM SCREENING QUESTIONNAIRE – ADAM QUESTIONNAIRE

ADAM QUESTIONNAIRE			
1	Do you have a decrease in libido (sex drive)?	Yes	No
2	Do you have a lack of energy?	Yes	No
3	Do you have a decrease in strength and/or endurance?	Yes	No
4	Have you lost height?	Yes	No
5	Have you noticed a decreased "enjoyment of life"	Yes	No
6	Are you sad and/or grumpy?	Yes	No
7	Are your erections less strong?	Yes	No
8	Have you noticed a recent deterioration in your ability to play sports?	Yes	No
9	Are you falling asleep after dinner?	Yes	No
10	Has there been a recent deterioration in your work performance?	Yes	No
If you Answer Yes to number 1 or 7 or if you answer Yes to more than 3 questions, you may have low Testosterone.			

6. FRAILTY SCREENING TOOL – FRAIL SCALE

FRAIL SCALE		
1.	"Have you felt fatigued? Most or all of the time over the past month?"	Yes No
2.	"Do you have difficulty walking one block?"	Yes No
3.	"Do you have difficulty walking one block?"	Yes No
4.	“Do you have any of these illnesses: hypertension, diabetes, cancer (other than a minor skin cancer), chronic lung disease, heart attack, congestive heart failure, angina, asthma, arthritis, stroke, and kidney disease?”) Five or greater = 1	Yes No
5.	“Have you lost more than 5 percent of your weight in the past year?”	Yes No

Frail – scores 3 to 5

Pre-frail - 1 to 2

Robust – 0

7. RAW DATA

Patientsnam	Ageofpatient	Stateofreside	Phonenumber	emailid	HospitalNum	Education	Occupation	Occupation	Incomeperm	tscoreneck	tscoreL1L4	tscoreradius	tbsscore	Serumtesto	hypotesto	Freetestoste	SHBG	Freetestoste	Freetestbin	Albumin	Diabetes	ACsugar	PCsugar	Hba1c	Randomsugar	Durationofd	Oralantidiab	Sulfonylurea	Glinides	SGLT2inhibi	Biguanides	thiazolidine	DPPIVinhibit
AMIN MAHT	70	JHARKHAND	8873527121	yogeshrajbk	331832H	High school certificate		Technicians	>52734	-2.4	0.6	-1.2	>1.3	408.00	0	15.08	93.620	3.910	1.00	4.08	0							0	0	0	0	0	0
PERUMALSA	69	TAMIL NADU	9487355887		387400h	High school certificate		Clerks	26355-52733					190.00	1	12.11	54.310	2.560	1.00	4.51	1	127	284	9.2		10	1	1	0	1	1	0	0
JAYACHANDR	67	TAMIL NADU			472843C	Middle scho	Plant & Machine Operat		13161-19758	-2.9	-2.7	-5.3	<1.2	279.00	1	27.53	35.070	5.150	0.00	4.51	1	93	276			12	1	1	0	0	1	0	1
JOSEPH S	83	TAMIL NADU			020526	Intermediate or diploma		Plant & Mac	19759-26354	-2.9	-2.4	-5.6	<1.2	471.00	0	19.26	84.600	5.120	0.00	3.74	0							0	0	0	0	0	0
GOVINDASA	79	TAMIL NADU	8760780575		419809f	Primary scho	Elementary Occupation		7887-13160	-1.9	-0.9	-2.7	<1.2	409.00	0	18.67	75.800	4.610	1.00	4.32	0							0	0	0	0	0	0
SOLOMON E	65	TAMIL NADU	9042880502	sebysamuel	096512P	High school	Plant & Mac	Plant & Mac	7887-13160	-2.8	-1.6	-1.1	<1.2	321.00	0	19.79	56.120	4.760	1.00	4.99	0							0	0	0	0	0	0
VAJJIRAVELU	66	TAMIL NADU	9449012192		744221C	High school certificate		Elementary	2641-7886	-1.8	-2.0	-1.7	1.2-1.3	368.00	0	27.80	45.800	5.860	0.00	4.58	0							0	0	0	0	0	0
RAMESHWA	65	JHARKHAND	8278721163	anandkumar	243043P	Illiterate		Elementary O	<2640	-2.4	-1.8	-1.9	1.2-1.3	279.00	1	30.75	31.400	5.660	0.00	4.25	0							0	0	0	0	0	0
RAMA CHAN	70	TAMIL NADU	9443639705		376482D	Graduate		Professionals	26355-52733	-2.7	-0.5	-1.6	1.2-1.3	177.00	1	8.24	74.300	1.900	1.00	4.30	1	169	228			11	1	1	0	0	1	0	0
KARTICK SHA	71	WEST BENGA	9475558881		031489P	Primary school certificat		Technicians	19759-26354	-1.4	-0.8	-2.2	<1.2	135.00	1	13.23	35.320	5.140	0.00	3.15	0							0	0	0	0	0	0
DHANAIAH T	65	ANDHRA PRA	9843855641		808868h	Illiterate		Elementary	2641-7886	-1.4	-2.7	-0.4	1.2-1.3	427.00	0	14.21	104.000	3.640	1.00	4.66	1	108	211			1	0	0	0	0	0	0	0
VELU.A	71	TAMIL NADU	9626959137		740030F	Primary school certificat		Elementary	2641-7886					172.00	1	6.56	90.700	1.630	1.00	3.62	1			6.5			0	0	0	0	0	0	0
GURUS	64	TAMIL NADU	9094849098		030795P	Primary school certificat		Elementary	2641-7886					474.00	0				0.00		1	144	281			1	1	0	0	0	1	0	0
JAGANATHA	72	ANDHRA PRA			260479P	High school	Elementary Occupation		2641-7886					359.00	0	11.46	108.400	2.920	1.00	4.52	1	174	380	6.8		10	1	0	0	0	1	0	0
EKAMBARAN	73	TAMIL NADU	9443309005		766772B	High school	Technicians and Associat		>52734					442.00	0	22.16	69.030	5.460	0.00	4.26	1			8.7		20	1	1	0	0	1	0	1
NATARAJAN	72	TAMIL NADU	9047979409		561553H	Intermediate or diploma		Technicians	26355-52733					264.00	1	35.66	25.620	5.630	0.00	4.70	1	125	398			10	1	1	0	0	1	0	0
VIJAYAKUMA	73	TAMIL NADU	9962080092		090695P	Middle school certificate		Elementary	2641-7886	-2.1	0.3	-4.4	<1.1	108.00	1	7.81	47.850	1.620	1.00	3.93	1			8.0		2	1	1	0	0	0	0	0
RAJENDRA P	72	JHARKHAND	8709199822	vikashbhada	248675d	High school	Skilled Workers and Sho		26355-52733	-1.3	-0.8	0.1	1.2-1.3	321.00	0	42.23	26.300	7.160	0.00	4.39	1	165	244			2	1	1	0	0	1	0	0
SIVANANTHA	76	TAMIL NADU	9943011204		849963B	High school certificate		Technicians	19759-26354					153.00	1	16.24	32.600	2.840	1.00	4.47	1	128	211			7	0	0	0	0	0	0	0
BIDYUT KUM	66	WEST BENGA	7679659173		099351p	Graduate		Technicians	26355-52733					138.00	1	9.07	52.630	1.850	1.00	4.65	0							0	0	0	0	0	0
ARUMUGAM	62	TAMIL NADU	9626770524		661401H	High school certificate		Technicians	26355-52733					214.00	1	30.09	24.610	4.720	1.00	4.46	1	129	268				1	1	0	1	1	0	0
SUNDARAMO	68	TAMIL NADU	9677571806	hemakumar	086506p	Primary scho	Elementary Occupation		7887-13160					149.00	1	20.71	24.900	3.110	1.00	4.68	1			9.3		2	1	0	0	0	0	0	0
RAVINDRA P	75	BIHAR	9110934445	sumansonu	244461p	Intermediate or diploma		Clerks	19759-26354					244.00	1	19.32	43.700	3.880	1.00	4.51	0							0	0	0	0	0	0
MUNIRATHN	82	ANDHRA PRA	8985320090	karnam.nav	061452A	Intermediate or diploma		Professionals	>52734					72.30	1	3.31	75.500	0.754	1.00	4.10	0							0	0	0	0	0	0
MD SAMSUL	68	BIHAR	8820151365		285074P	Illiterate		Skilled Agric	7887-13160					20.00	1	1.66	12.040	0.598	1.00	3.96	1			6.5		1	1	0	0	0	1	0	0
ZACHARIAH S	78	TAMIL NADU			805286b	High school certificate		Clerks	19759-26354					290.00	1	13.67	73.400	3.410	1.00	3.58	1			6.9		1	0	0	0	0	0	0	0
IQBAL.A	71	TAMIL NADU	9789691110	esranahmed	321122g	Middle school certificate		Plant & Mac	26355-52733	-2.1	-2.1	-1.5		152.00	1	22.14	23.760	3.380	1.00	4.35	1	123	220	11.4		21	1	1	0	0	1	0	0
JAGO MAND	64	JHARKHAND	8298236419	grdnet.1955@	065884P	Intermediate	Skilled Work	Skilled Work	>52734	-0.7	-1.6	0.5	<1.2	274.00	1	23.82	39.810	4.760	1.00	4.31	0							0	0	0	0	0	0
IQBAL.A	71	TAMIL NADU	9789691110		321122p	Illiterate		Elementary	2641-7886					173.00	1	19.01	31.490	3.710	1.00	4.64	1	123	246	6.4		6	1	1	0	0	1	0	0
NAOSAR SAR	61	WEST BENGA	9088627616	Rintusajid@	211571P	Illiterate	Elementary Occupation		2641-7886	-2.9	-4.3	-3.1	<1.2	460.00	0	14.67	64.220	6.050	0.00	4.25	1	97	204			1	1	1	0	0	0	0	0
ASHOK KUM	60	BIHAR	7070427193	aksah00371	340101P	Middle scho	Technicians and Associat		>52734	-1.6	-3.2	-1.7	>1.3	479.00	0	42.61	38.900	9.060	0.00	4.31	0							0	0	0	0	0	0
JOYDEV BISW	66	WEST BENGA	9732750905	mistubiswa	215272h	Graduate	Elementary Occupation		19759-26354	-2.5	-2.5	-2.1	1.2-1.3	281.00	1	15.26	63.700	3.410	1.00	4.72	1			6.7		4	1	0	0	0	1	0	0
SUSHIL ROY	69	WEST BENGA	6294471824		033177P	High school certificate		Technicians	19759-26354	-0.6	-1.4	-2.2	1.2-1.3	607.00	0	29.61	70.930	7.540	0.00	4.53	0							0	0	0	0	0	0
SARAT KUMA	62	WEST BENGA	9434054836	alfatravels0	692530h	High school certificate		Clerks	7887-13160	0.4	-0.7	0.9	>1.3	533.00	0	32.76	56.300	7.950	0.00	4.25	1	130	219	9.1		2	1	0	0	0	1	0	0
SREEPADA SA	83	WEST BENGA	7980244856	DEBASISHSA	032423P	Graduate		Technicians	26355-52733					342.00	0	6.10	194.000	1.670	1.00	4.07	0							0	0	0	0	0	0
PRADIP MAJU	64	WEST BENGA	9800920134		993016G	Intermediate	Skilled Workers and Sho		13161-19758					383.00	0	40.50	32.720	7.580	0.00	4.56	1	256	453	8.9		4	1	1	0	0	1	1	0
SRINIVASAN	72	TAMIL NADU	9047147800	saravanansr	692422D	Graduate		Clerks	26355-52733					478.00	0	21.88	75.600	5.570	0.00	4.17	1	89	203			1	1	1	0	0	0	0	0
MANICKAM	68	TAMIL NADU	9688748849		026883P	Illiterate		Elementary	2641-7886					225.00	1	14.56	53.460	3.210	1.00	4.04	0							0	0	0	0	0	0
MARKONDA	81	ANDHRA PRA	9963903638		510095P	Illiterate		Elementary	2641-7886					480.00	0	23.99	69.220	5.970	0.00	4.29	0							0	0	0	0	0	0
MUTHUSAM	63	TAMIL NADU	9965020016	msathesh05@	087762p	Intermediate	Craft & Related Trade W		>52734	-1.2	-0.2	-2.4	>1.2	421.00	0	21.55	67.590	5.010	0.00	4.92	0							0	0	0	0	0	0
MAHABOOB	67	ANDHRA PRA	9985557102		205491G	Primary school certificat		Elementary	2641-7886	-1.3	-0.3	-1.1	>1.3	170.00	1	25.11	23.430	3.710	1.00	4.63	1	96	236			13	1	1	0	0	1	0	0
BINOD KUMA	62	JHARKHAND	7631060001	Kristinapriya	010721P	Intermediate	Skilled Workers and Sho		>52734	-1.3	-1.6	0.1	<1.2	318.00	0	26.20	42.000	5.460	0.00	4.24	0							0	0	0	0	0	0
EKAMBARAM	64	TAMIL NADU	9787087005	shrivijay.300	775636G	Intermediate or diploma		Elementary	2641-7886	-0.8	-0.6	1.0	>1.3	314.00	0	34.82	31.200	6.160	0.00	4.68	0							0	0	0	0	0	0
KRISHNA PAD	65	WEST BENGA	99339804020		235765P	Intermediate	Technicians and Associat		>52734					422.00	0	16.50	88.520	4.130	1.00	4.60	0							0	0	0	0	0	0
DORAIRAJ A	71	TAMIL NADU	9345300156		038073P	Profession or Honours		Professionals	>52734	-0.1	1.5	-2.9	>1.3	160.00	1	17.03	32.500	3.490	1.00	4.81	1	131	357	8.0		15	1	1	0	0	1	0	0
GOVIND PRA	64	BIHAR	9065581610	Rengali1979@	025321P	High school certificate		Skilled Work	26355-52733	-0.1	-0.5	-1.3	<1.2	132.00	1	15.66	29.160	2.660	1.00	4.21	1	178	253			5	1	1	0	0	1	0	0
SIVAKUMAR	67	TAMIL NADU			518861B	High school	Craft & Related Trade W		7887-13160					187.00	1	19.67	32.900	3.670	1.00	4.00	1	192	255			16	1	1	0	1	1	0	1
SUBRAMANI	74	TAMIL NADU	9092583390		213430P	Illiterate		Elementary	2641-7886	-1.8	-1.5	-0.9	>1.3	383.00	0	35.72	37.100	7.240	0.00	4.29	0							0	0	0	0	0	0
SUNDARA RA	66	TAMIL NADU	9677393526	unnask90@	287570P	Middle school certificate		Elementary	2641-7886					222.00	1	21.28	36.100	4.240	1.00	3.84	0							0	0	0	0	0	0
SK SAIFUDDI	66	WEST BENGA	9101229084	ajkk0657122	248937p	High school certificate		Skilled Work	19759-26354					564.00	0	23.48	83.100	6.060	0.00	4.55	0							0	0	0	0	0	0
KANKA MAH	68	WEST BENGA	9002218852		236228p	Primary scho	Elementary Occupation		13161-19758					589.00	0	23.37	87.200	6.130	0.00	4.52	0						0	0	0	0	0	0	0
BALAIAH P	71	TAMIL NADU	9941806092		515822P	High school certificate		Skilled Work	26355-52733	-3.6	-3.4	-3.9	<1.2	482.00	0	23.13	72.100	1.650	1.00	4.01	1			9.7			1	1	0	0	1	0	0
BAHADUR RA	63	JHARKHAND	9798979801		269337p	High school certificate		Skilled Work	13161-19758	-3.0	-4.6	-3.6	1.2-1.3	554.00	0	44.89	42.700	10.200	0.00	4.25	1	173	268			2	1	1	0	0	1	0	0
HANS KUMA	60	BIHAR	7004021856		243721P	Graduate		Professionals	>52734	-1.3	-1.4	-2.9	1.2-1.3	498.00	0	17.62	97.800	4.530	1.00	4.73	0							0	0	0	0	0	0
MAHABIR M	61	JHARKHAND	6205133545	kdkumar101	057121p	High school	Elementary Occupation		7887-13160	-1.1	-3.7	-1.4	<1.2	804.00	0	42.71	65.140	11.500	0.00	4.36	1					10	1	1	0	0	1	0	0
RAGHUPATI	79	WEST BENGA	7003402147		089074P	Illiterate		Elementary	2641-7886	-1.3	-2.9	-2.1	<1.2	200.00	1	22.46	30.810	3.910	1.00	4.43	1			7.5		10	1	1	0	0	1	1	0
RAMAKRISHN	61	TAMIL NADU	9865984003		258869P	High school certificate		Elementary	7887-13160	-1.4	-3.0	-2.3	<1.2	456.00	0	18.94	83.300	4.680	1.00	4.79	0							0	0	0	0	0	0
MAHESH PRA	66	BIHAR	8699108804		244111p	Graduate		Technicians	>52734	-1.4	-1.6	-1.0	1.2-1.3	213.00	1	21.06	35.000	3.840	1.00	4.53	0							0	0	0	0	0	0
TAPAS KUMA	75	WEST BENGA	9831224995		230910d	High school certificate		Skilled Work	13161-19758	-1.7	-1.6	-1.6	<1.2	232.00	1	21.70	37.000	3.900	1.00	4.99	0							0	0	0	0	0	0
JAMBULINGA	80	TAMIL NADU	9626456532		999857h	High school certificate		Professionals	19759-26354	-1.3	-1.5	-2.3	1.2-1.3	316.00	0	13.89	78.700	3.380	1.00	4.29	1	114	235			21	1	1	0	0	1	0	0
HRIDAY CHA	62	WEST BENGA	9339221839		098640P	High school certificate		Skilled Work	7887-13160	-2.1	-1.8	-1.5	<1.2	388.00	0	24.02	55.890	5.450	0.00	4.49	0							0	0	0	0	0	0
SWAPAN KU	65	JHARKHAND	7870604039		248284f	Graduate		Professionals	>52734	-1.8	-1.0	-2.0	>1.3	598.00	0	23.17	89.300	6.070	0.00	4.63	0						0	0	0	0	0	0	0
DEENADAYA	71	TAMIL NADU	9443803982		265668F	Illiterate		Elementary	2641-7886	-1.3	-0.5	-2.0	>1.3	107.00	1	8.05	46.000	1.650	1.00	3.89	0	136	154			11	1	1	0	0	0	0	0
THANGAVEL	80	TAMIL NADU	7639729984		286019P	Illiterate		Elementary	2641-7886	-1.4	-0.4	-1.6	1.2-1.3	392.00	0	20.65	65.700	4.890	1.00	4.44	1	104	255			1	1	1	0	0	1	0	0
JAYARAJAN.	74	TAMIL NADU			570387B	Primary school certificat		Skilled Work	26355-52733	-1.8	-2.1	1.1	<1.2	245.00	1	25.53	33.200	4.720	1.00	4.31	0							0	0	0	0	0	0
MUNIRATINA	80	TAMIL NADU	9786926050		859552D	Middle scho	Elementary Occupation		7887-13160	-1.6	-1.8	-0.5	1.2-1.3	330.00	0	19.00	60.110	4.460	1.00	4.05	1					11	1	0	0	0	1	0	0
SUBRAMANI	61	TAMIL NADU	9842820978		988933H	Primary school certificat		Elementary	2641-7886	-1.8	-1.6	0.9	>1.3	234.00	1	23.27	34.790	4.340	1.00	4.37	1	217	347			1	1	1	0	0	1	0	0
SANAT KUM	64	WEST BENGA	9836978427		089694P	Middle scho	Elementary Occupation		13161-19758	-1.7	-1.6	-0.8	1.2-1.3	337.00	0	18.21	64.020	4.080	1.00	4.93	0							0	0	0	0	0	0
DHANAPAL K	69	TAMIL NADU	8489172826		651735h	Primary scho	Elementary Occupation		2641-7886	-0.6	-2.3	-0.2	1.2-1.3	125.00	1	19.39	22.310	2.980	1.00	3.98	0							0	0	0	0	0	0
RAJENDRA B	71	TAMIL NADU	9940237839		892436h	High school certificate		Elementary	13161-19758	-0.7	-1.5	0.4		216.00	1	37.56	19.900	5.170	0.00	4.59	1			6.7		2	1	0	0	0	1	0	0
SWAPAN CH	65	WEST BENGA	8001521456	chatterjeega	285244P	Graduate		Skilled Work	19759-26354	-1.6	-0.1	0.6	1.2-1.3	485.00	0	32.65	51.400	7.230	0.00	4.84	0							0	0	0	0	0	0
LAKSHMANA	61	TAMIL NADU	9345772265		256816P	Primary school certificat		Elementary	2641-7886	-1.6	1.1	-0.2	>1.2	151.00	1	17.67	29.570	3.270	1.00	3.59	1		254	11.2		1	1	0	0	0	1	0	1
SELVARAJ	64	TAMIL NADU	4162215623		911655g	High school	Skilled Workers and Sho		19759-26354	-0.5	0.8	-0.3	1.2-1.3	205.00	1	24.35	29.130	4.130	1.00	4.45	1	109	202	7.2		1	1	0	0	0	1	0	0
RUTHIRAN	71	TAMIL NADU	7538829808		285503P	High school certificate		Skilled Work	19759-26354	1.2	1.8	1.9	>1.3	250.00	1	25.37	34.100	4.570	1.00	4.68	1			7.2		30	1	0	0	0	1	0	0
GAURHARI G	63	WEST BENGA	9732523549		842836H	Illiterate		Skilled Work	7887-13160	1.0	0.5	-0.3	>1.3	425.00	0	31.03	47.400	6.650	0.00	4.71	0							0	0	0	0	0	0
SIVAPRAKAS	61	TAMIL NADU	8838539766		226723p	High school	Skilled Workers and Sho		7887-13160	-0.8	-0.4	-0.9	1.2-1.3	316.00	0	29.39	37.200	5.940	0.00	4.12	1	209	355			20	1	1	0	0	1	0	0
OM PRAKASH	63	UTTAR PRAD	9852391553	sonamjaisw	248826p	High school	Technicians	Technicians	19759-26354	-0.1	-0.8	-0.6	>1.3	331.00	0	31.38	36.500	6.100	0.00	4.46	1		315		379	10	1	1	0	0	1	0	1
DHAYALAN A	65	TAMIL NADU	8762209465		412192H	Primary scho	Elementary Occupation		2641-7886	-0.2	-0.7	-0.6	>1.3	280.00	1	22.46	34.140	5.120	0.00	4.76	1	113	272			6	1	1	0	0	1	0	1
SAMIKANNU	64	TAMIL NADU	9442219457		237401P	Profession o	Professionals		26355-52733	-1.5				294.00	1	37.65	27.020	6.520	0.00	4.25	1	135	250	6.8		2	1	1	0	0	1	0	0
WAKIL PRASA	72	JHARKHAND	8864025472		285237P	High school certificate		Technicians	26355-52733					220.00	1	26.52	28.700	4.510	1.00	4.41	1	179	230	6.8		1	0	0	0	0	0	0	0
ANBALAGAN	69	TAMIL NADU	9003483197		251549f	Primary scho	Elementary Occupation		7887-13160					244.00	1	19.32	43.700	3.880	1.00	4.51	1	105	155	9.1		15	1	1	0	0	1	0	0
PALANI	67	TAMIL NADU			964466B	High school certificate		Elementary	2641-7886					310.00	0	22.64	47.370	4.680	1.00	4.73	1			6.7		1	1	0	0	0	1	0	0
SUBHASH CH	75	WEST BENGA	9830695053	subrata.saha	239054p	Intermediate or diploma		Skilled Work	26355-52733					225.00	1	16.22	48.000	3.350	1.00	4.45	1	143	163	7.0		1	1	0	0	0	1	0	0
VISHWANAT	65	JHARKHAND	8340172924	singhmanish	848932h	Graduate		Professionals	26355-52733					259.00	1	36.28	24.700	5.900	0.00	4.31	1	107	152			11	1	1	0	0	1	0	0
KALYAN BAN	72	WEST BENGA	9832192061		762711d	High school certificate		Professionals	26355-52733					377.00	0	26.14	47.200	6.030	0.00	4.35	1	121	117	6.4		3	1	1	0	0	0	0	0
GUNA SINDH	70	WEST BENGA			221116P	Illiterate		Elementary	2641-7886					299.00	1	20.82	49.700	4.520	1.00	4.29	0							0	0	0	0	0	0
KUMARAVEL	64	TAMIL NADU	8667769178		239755p	Intermediate	Skilled Agric	Skilled Agric	19759-26354					200.00	1	15.69	44.100	3.190	1.00	4.25	0							0	0	0	0	0	0
PROBHAS KU	62	WEST BENGA			097756P	High school certificate		Technicians	19759-26354					360.00	0	19.99	62.310	4.620	1.00	4.50	0							0	0	0	0	0	0
KHANDU GIR	71	WEST BENGA	9064152070	Santanud16	256292p	Graduate	Technicians	Technicians	>52734					411.00	0	20.19	70.450	4.830	1.00	4.59	0							0	0	0	0	0	0
ANTHONI MA	61	TAMIL NADU	9791771320		235169P	Primary scho	Plant & Machine Operat		7887-13160					214.00	1	21.66	36.270	3.760	1.00	4.59	1	124	234	7.6		1	1	0	0	0	1	0	0
SEWA SAW	61	JHARKHAND	8340231070	anilkumar.sa	242496p	Intermediate or diploma		Skilled Work	26355-52733					148.00	1	24.98	20.500	3.340	1.00	4.78	1	276	383	11.4		2	1	1	0	0	1	0	0
DHANANJOY	62	WEST BENGA	9734210412		275908p	High school certificate		Elementary	2641-7886					334.00	0	28.12	41.100	5.660	0.00	4.57	0							0	0	0	0	0	0
MAHADEO P	72	JHARKHAND	9576671219		254489p	Intermediate	Clerks	Clerks	26355-52733				<1.2	288.00	1	33.78	29.500	5.840	0.00	4.58	0							0	0	0	0	0	0
NEPAL DAS	66	WEST BENGA	7384250061	nepaldas40	287519P	Middle scho	Craft & Related Trade W		13161-19758					550.00	0	29.88	63.700	7.240	0.00	4.67	0							0	0	0	0	0	0
MANOJ KUM	60	WEST BENGA	9378278027		236426P	Intermediate or diploma		Technicians	>52734					228.00	1	34.03	23.180	5.690	0.00	3.79	0							0	0	0	0	0	0
ANDREWS	60	TAMIL NAD			243002A	Primary school certificat		Elementary	7887-13160					297.00	1	28.16	36.500	5.380	0.00	4.51	1	161	179	7.5		10	1	0	0	0	1	0	0
NAND KISHO	64	JHARKHAND	9304844218		268743P	Graduate		Professionals	>52734					304.00	0	22.85	46.040	4.630	1.00	4.83	0							0	0	0	0	0	0
ANNAMALAI	66	TAMIL NADU	9488682703		277363p	High school certificate		Elementary	2641-7886					143.00	1	26.14	18.930	3.450	1.00	4.51	1	176	229			21	1	1	0	0	0	0	1
SUNDARARA	72	TAMIL NADU			874052b	High school certificate		Clerks	26355-52733					348.00	0	22.42	53.700	4.970	1.00	4.49	1	145	236			3	1	0	0	0	1	0	0
RAMA CHAN	74	TAMIL NADU	9159456849		809335F	Intermediate or diploma		Plant & Mac	26355-52733					255.00	1	18.12	48.700	3.810	1.00	4.42	1	133	180	7.2		6	1	1	0	0	1	0	1
MAHALINGA	70	TAMIL NADU	9443533530		261591P	Intermediate or diploma		Elementary	2641-7886					518.00	0	27.92	64.200	7.020	0.00	4.11	1	159	414	6.9		7	1	0	0	0	1	0	0
SHAMBHUNA	64	WEST BENGA	8525842888		285205P	Middle school certificate		Elementary	2641-7886					288.00	1	42.77	23.300	6.400	0.00	4.80	1	125	158	9.2		5	1	0	0	0	1	0	0
KOPPOLU SO	62	ANDHRA PRA	9398323765	SOLOMONK	097978P	High school certificate		Technicians	26355-52733	-2.1	-2.3	-2.1	<1.2	172.00	1	11.60	51.300	2.330	1.00	4.87	0							0	0	0	0	0	0
GOVIND KUM	64	BIHAR	9994321636	rengali1979@	058686F	High school	Technicians and Associat		26355-52733	-1.2	-2.0	-1.2	1.2-1.3	214.00	1	26.79	27.640	4.390	1.00	4.57	1		326	8.0		6	1	1	0	0	1	1	0
SUBODH KUM	60	JHARKHAND	9334232371	hirapanna04	259417p	Graduate	Skilled Workers and Sho		26355-52733	-1.5	-2.0	-1.1	1.2-1.3	224.00	1	19.57	39.600	3.730	1.00	4.63	1	119	149	6.1		1	1	0	0	0	1	0	0
ARUNACHAL	66	ANDHRA PRA	9399959962		384388g	Primary scho	Skilled Workers and Sho		19759-26354	-1.5	-1.5	-1.7	<1.2	328.00	0	35.03	32.400	3.900	1.00	4.83	1	142	206	6.9		11	1	1	0	0	1	0	0
BHOLI BABU	62	BIHAR	9472396831	mcp.estrail@	092160p	High school	Skilled Workers and Sho		26355-52733	-1.9	-1.2	-1.9	<1.2	427.00	0	25.74	57.400	5.830	0.00	4.74	0							0	0	0	0	0	0
GANESAN C.	69	TAMIL NADU	9715091154		093469p	Middle scho	Elementary Occupation		7887-13160	-0.7	-1.4	-1.1	<1.2	189.00	1	15.06	43.420	2.970	1.00	4.48	1	118	144			1	1	0	0	0	1	0	0
DAVID. M.	69	TAMIL NADU	7092055092		873981H	Primary scho	Craft & Related Trade W		7887-13160	-0.9	-1.5	-1.9	<1.2	345.00	0	12.50	27.510	7.780	0.00	4.18	0							0	0	0	0	0	0
NIKHIL CHAN	73	TRIPURA	9436952450		568481c	Graduate		Professionals	>52734	0.1	0.3	-2.5	>1.3	246.00	1	22.20	38.350	4.180	1.00	4.68	1	122	237	6.8		13	1	1	0	0	1	0	0
SAMASIVAM	78	TAMIL NADU	9025603166		434858G	High school certificate		Elementary	2641-7886	-0.8	0.9	-1.7	1.2-1.3	360.00	0	16.58	75.130	5.140	0.00	4.11	1	146	227	9.4		10	1	1	0	0	1	0	0
DHAMODHA	69	ANDHRA PRA	9705695665		746396F	Middle school certificate		Technicians	26355-52733	-0.6	0.6	-2.3	1.2-1.3	258.00	1	36.44	24.500	5.440	0.00	4.96	1	159	351	7.2		11	1	1	0	0	1	1	1
DEIVASIGAM	69	TAMIL NADU	9952600910		237655p	Primary scho	Elementary Occupation		2641-7886	-1.8	-1.9	-0.3	1.2-1.3	326.00	0	15.57	72.440	3.710	1.00	4.40	1	117	231	6.7		15	1	1	0	0	1	0	0
MANOHARA	62	TAMIL NADU	8340207176		848152H	High school certificate		Elementary	7887-13160	-0.3	-1.1	-0.2	1.2-1.3	219.00	1	29.01	26.120	4.500	1.00	4.82	1	215	269	10.8		5	1	1	0	0	1	0	1
GNANAPRAK	72	TAMIL NADU			589677	Intermediate or diploma		Technicians	26355-52733	-1.1	2.3	0.8	>1.3	414.00	0	22.28	64.310	5.270	0.00	4.49	1	205	288	10.0		7	1	1	0	0	1	1	1
ENGAIH MAN	68	TAMIL NADU	9698421141		157441h	Illiterate	Elementary Occupation		7887-13160	-1.3	-0.5	-0.8	<1.2	163.00	1	12.23	46.100	2.440	1.00	4.46	1	132	189	7.2		6	1	0	0	0	1	0	0
RADHA KRISH	66	TAMIL NADU	9486083153		235686p	Primary scho	Elementary Occupation		2641-7886	-1.0	1.9	-0.8	>1.3	256.00	1	15.58	56.860	3.360	1.00	4.66	1		180	6.5		1	1	0	0	0	1	0	0
PHANI HAZRA	62	WEST BENGA	9330381307	Monsterboo	215032p	Graduate	Skilled Workers and Sho		19759-26354	0.3	0.5	-0.7	>1.3	317.00	0	33.96	32.300	6.210	0.00	4.52	0							0	0	0	0	0	0
VEERASAMY	67	TAMIL NADU	9994990541		934427G	High school certificate		Skilled Work	26355-52733	-0.1	0.6	-0.8	>1.3	206.00	1	17.25	41.330	3.380	1.00	4.41	1		218	6.5		1	0	0	0	0	0	0	0
SARANGAPA	66	TAMIL NADU	9382809369		095335P	Primary school certificat		Elementary	13161-19758	-0.3	0.3	1.1	>1.3	177.00	1	24.40	25.100	3.720	1.00	4.69	1	206		7.8		6	1	1	0	0	1	0	0
MANOHARA	66	TAMIL NADU	9944486408	manoharan	742821d	Profession or Honours		Professionals	>52734	0.6	1.5	-0.5	1.2-1.3	312.00	0	20.22	53.400	4.430	1.00	4.47	1			7.2		3	1	1	0	0	1	0	0
KARUNAGAR	66	TAMIL NADU	9443696678		163596G	High school certificate		Professionals	26355-52733	0.8	1.8	-0.2	>1.3	192.00	1	27.23	24.400	4.320	1.00	4.27	1			7.5		20	1	1	0	0	1	0	0
VENKATESAN	74	TAMIL NADU	9940799110		110059h	Middle school certificate		Elementary	7887-13160	1.3	1.7	-0.2	>1.3	717.00	0	59.87	41.440	13.900	0.00	4.44	1	142	236			4	1	1	0	0	1	0	1
NIKHIL CHAN	62	WEST BENGA	9474343243		031486P	Profession or Honours		Professionals	>52734	-0.2	-0.8	-0.4	1.2-1.3	444.00	0	38.76	39.640	7.330	0.00	5.39	1	129				11	1	0	0	0	1	0	0
DAYALAN V.	72	TAMIL NADU	9095847419		985964d	Illiterate	Elementary Occupation		2641-7886					129.00	1	21.77	20.500	3.160	1.00	4.10	0							0	0	0	0	0	0
RAJAMANI D	62	TAMIL NADU	8098999502		992673H	High school	Elementary Occupation		7887-13160					173.00	1	14.67	40.800	2.890	1.00	4.19	1			6.6			0	0	0	0	0	0	0
SUNDARAMU	70	TAMIL NADU	9442261946		054139f	High school certificate		Professionals	26355-52733					243.00	1	16.44	51.150	3.520	1.00	4.33	1			6.7			1	1	0	0	1	0	0
RAJ KUMAR	69	WEST BENGA	9434011545	ca.bagaria@	928824D	Graduate		Technicians	>52734					258.00	1	23.68	37.700	4.840	1.00	3.87	1	113	174	8.2		3	1	0	0	0	1	0	0
JEYASEELAN	62	TAMIL NADU			268167D	High school	Craft & Related Trade W		7887-13160					247.00	1	34.74	24.600	5.320	0.00	4.75	1	141	172	11.2		15	1	0	0	0	1	0	0
ABDUL JALIL	61	WEST BENGA	8017442350		024569p	Primary school certificat		Elementary	7887-13160					328.00	0	28.39	39.980	5.640	0.00	4.57	0							0	0	0	0	0	0
SHYAMAL HA	65	WEST BENGA	7047537116		098503p	Middle school certificate		Elementary	7887-13160					205.00	1	28.71	24.710	4.620	1.00	4.25	0					1		0	0	0	0	0	0
RADHAKRISH	67	TAMIL NADU	8608279750		825208h	Primary scho	Skilled Workers and Sho		7887-13160					203.00	1	19.90	35.300	3.660	1.00	4.44	1	112	276	7.7		2	1	0	0	0	1	0	0
SOUNDARAB	69	TAMIL NADU	9443803856	SOUNDARAB	347678a	Intermediate or diploma		Technicians	26355-52733					212.00	1	31.22	23.500	4.860	1.00	4.33	1	276	383	11.4		20	1	1	0	0	1	0	1
PACHIAPPAN	69	TAMIL NADU	9442154986	taxman.pon	548787a	High school	Technicians	Technicians	26355-52733					249.00	1	22.95	37.540	4.270	1.00	4.74	1	165	220	7.0		25	1	1	0	0	1	0	0
SEKAR	61	TAMIL NADU	9465258256		764527H	Middle scho	Skilled Agric	Skilled Work	19759-26354					262.00	1	23.37	38.800	4.450	1.00	4.67	1			6.7		2	1	1	0	0	1	0	0
RAMADOSS.	76	TAMIL NADU	9843475813		005545f	High school	Elementary Occupation		13161-19758					175.00	1	26.44	22.900	4.230	1.00	3.93	1	203	300	8.1		12	1	1	0	0	1	0	1
DEVANBU Y.	63	TAMIL NADU	7708113430		295329P	High school	Professionals		19759-26354					489.00	0	27.38	61.800	6.490	0.00	4.64	0							0	0	0	0	0	0
SUNDARRAJA	68	TAMIL NADU	9865369705		421881h	Profession or Honours		Legislators, S	>52734					173.00	1	21.91	27.320	5.940	0.00	4.19	1	104	134	6.5			1	1	0	0	1	0	1
JAYAPAL.T.N	69	ANDHRA PRA			365543b	High school	Professionals	Professionals	26355-52733					247.00	1	23.94	35.700	4.380	1.00	4.70	1			10.1		25	1	0	0	0	1	0	1
DAYYAIA RAM	70	ANDHRA PRA	9652857811		510980P	Middle scho	Skilled Workers and Sho		13161-19758					156.00	1	23.68	22.800	5.970	0.00	4.56	0							0	0	0	0	0	0
DHANUSKOD	66	TAMIL NADU	9025555051		811010F	Illiterate		Craft & Relat	7887-13160					361.00	0	19.73	63.300	4.710	1.00	4.12	0							0	0	0	0	0	0
RATHINAMA	65	TAMIL NADU	9486327127		402923H	High school certificate		Professionals	26355-52733					266.00	1	27.89	33.000	4.970	1.00	4.70	0							0	0	0	0	0	0
KANTHAN S.	61	TAMIL NADU	9442249957		810657G	Graduate		Technicians	>52734					233.00	1	233.00	34.790	4.370	1.00	4.25	0							0	0	0	0	0	0
ARABINDRA	68	ASSAM	9954520554		778064F	Intermediate or diploma		Technicians	26355-52733	-1.3	-2.7	-3.7	<1.2	429.00	0	21.67	68.500	5.140	0.00	4.70	0							0	0	0	0	0	0
PRABHAKARA	68	TAMIL NADU	9443007489		794990F	Graduate		Professionals	>52734	-1.5	0.6	-1.6	1.2-1.3	152.00	1	18.01	29.200	3.030	1.00	4.37	1			7.5		25	1	1	0	0	1	0	1
MATHEW .S	65	TAMIL NADU	9751741101		000214A	Middle school certificate		Elementary	13161-19758	-1.4	0.3	-1.2	1.2-1.3	189.00	1	22.79	28.700	3.870	1.00	4.33	1	109	163	6.5		12	1	1	0	0	1	0	0
LAKSHMIGHA	72	TAMIL NADU	9486840315		971531D	Middle scho	Skilled Workers and Sho		26355-52733	-1.2	2.6	0.5		146.00	1	8.01	63.100	1.800	1.00	4.03	0						0	0	0	0	0	0	0
JANAKIRAMA	67	TAMIL NADU	9443542981		270190P	Middle school certificat		Skilled Work	7887-13160	-0.9	-0.5	-0.1	>1.3	401.00	0	29.00	47.850	6.250	0.00	4.61	1	154	146			11	1	1	0	0	0	0	0
HARIKRISHN	71	TAMIL NADU	9047672505		817706h	High school	Technicians	Technicians	26355-52733	-0.7	3.3	-0.5	>1.3	190.00	1	28.96	22.700	4.200	1.00	4.70	1	110	208			5	1	1	0	0	1	0	1
DEENADAYA	77	TAMIL NADU			923228b	High school certificate		Technicians	26355-52733	0.1	1.2	-0.6	1.2-1.3	98.00	1	9.03	37.540	1.630	1.00	4.53	0							0	0	0	0	0	0
ARULDAS	66	TAMIL NADU	8754650174		589770H	High school certificate		Clerks	19759-26354	-0.3	0.2	-0.7	1.2-1.3	1133.00	0	90.08	43.520	21.900	0.00	5.05	1	123	193	10.7		18	1	1	0	0	1	1	0
CHANDRASH	60	JHARKHAND	9835158043		215607P	Graduate		Technicians	>52734	1.6	1.8	-0.9	>1.3	224.00	1	34.91	22.200	5.300	0.00	4.33	1		148	7.2		35	1	1	0	0	1	1	1
THANGA RAJ	62	TAMIL NADU			738395D	High school certificate		Technicians	26355-52733					177.00	1	20.06	30.530	3.500	1.00	4.29	0							0	0	0	0	0	0
WILLIAMS	72	TAMIL NADU			668194	Graduate		Professionals	26355-52733					142.00	1	25.46	19.300	3.240	1.00	4.89	1		153	6.6		11	1	1	0	0	1	0	1
YESU PATHA	67	TAMIL NADU	9442223727		593254h	High school certificate		Professionals	13161-19758					319.00	0	23.34	47.300	4.810	1.00	4.78	1	117	221			3	1	0	0	0	1	0	0
MOHAMMED	61	CHATTISGAR	9009129433		248677p	High school	Skilled Workers and Sho		26355-52733					238.00	1	32.04	25.700	5.150	0.00	4.51	0							0	0	0	0	0	0
CHANDRASE	62	TAMIL NADU	9442815869		098653P	Intermediate or diploma		Technicians	19759-26354					203.00	1	24.93	28.180	3.970	1.00	4.88	1					3	1	0	0	1	1	0	0
CHANDRAN.R	61	TAMIL NADU	9628380308		331896c	Graduate		Professionals	26355-52733					26.77	1	26.77	38.000	5.160	0.00	4.58	1	153	245	7.8		15	1	1	0	0	1	1	0
RAJENDRAN.	70	TAMIL NADU	9600252909		285421F	Middle scho	Skilled Workers and Sho		19759-26354					221.00	1				0.00	4.40	1		278			11	1	1	0	0	1	0	0

glucosidas	Insulin	Hypertensi	Durationof	ACEi	ARB	betablocke	CCB	Thiazidedi	alphablock	Otherdiure	Cardiovasc	ECGchange	HistoryofM	CABGinthe	Heart	Strokeinth	Dyslipidem	COPD	Hypothyro	Parkinsons	Others	Others1	Tscoreoste	TBSscore_	Height	Weight	BMI	BMIclass	Overweigh	Smoking	Currentorp	Numberof	Alcoholinta
0		1	16	0	1	0	0	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0	OSTEOART			172.00	53.00	17.92	-1.00	0.00	0			1
0	0	1	1	1	0	1	0	0	0	1	1	1	1	0	1.00	0	1	0	0	0	0				170.00	50.00	17.30	-1.00	0.00	0			0
0		1	4	0	0	0	1	0	0	0	0	0	0	0	0.00	0	1	1	0	0	0				161.00	61.00	23.53	0.00	0.00	1	Past smoke	35	1
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				162.00	65.10	24.81	0.00	0.00	1	Past smoke	10	1
0		1	8	1	0	1	0	0	0	1	1	1	0	0	1.00	0	1	1	0	0	1	CCF			161.00	52.70	20.33	0.00	0.00	1	Past smoke	80	1
0		1	4	0	0	0	0	0	0	0	1	0	0	0	0.00	1	0	1	0	0	0				174.00	63.00	20.81	0.00	0.00	1	Past smoke	35	1
0		1		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	1	ASTHMA, A			164.00	51.00	18.96	0.00	0.00	1	Past smoke	25	1
0		1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	1	OSTEOART			166.00	60.00	21.77	0.00	0.00	0			0
0	0	1	6	0	0	1	1	0	0	0	0	0	0	0	0.00	0	0	0	0	1	0				165.00	62.00	22.77	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				155.00	47.40	19.73	0.00	0.00	1	Past smoke	35	
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				158.00	48.66	19.49	0.00	0.00	0			0
0	0	1	1	0	0	0	0	0	0	1	1	1	0	0	1.00	0	0	1	0	0	0	HEART FAII			160.00	52.00	20.31	0.00	0.00	1	Past smoke	50	1
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				160.00	56.90	22.23	0.00	0.00	1	Past smoke	30	1
0	0	1	6	0	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0	PAOD			163.00	53.00	19.95	0.00	0.00	0			0
0	0	1	15	0	1	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	1	0				158.00	52.80	21.15	0.00	0.00	0			0
0	0	1	2	0	1	0	1	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0	EXTRAPYRA			177.00	71.40	22.79	0.00	0.00	1	Current sm	30	1
0	0	1	11	0	0	1	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				168.00	76.00	26.93	1.00	1.00	1			0
0	0	1	8	0	1	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				166.00	72.00	26.13	1.00	1.00	1			0
0	0	1	8	1	0	0	0	0	0	0	0	0	1	0	1.00	0	1	0	0	0	0				175.00	82.90	27.07	1.00	1.00	1	Past smoke	20	1
0		1	1	0	0	0	1	0	0	0	1	1	0	0	1.00	0	0	0	0	0	0				169.00	72.80	25.49	1.00	1.00	0			0
0	0	1		0	0	1	1	0	0	0	1	0	1	0	1.00	1	1	0	0	0	0				173.00	78.40	26.20	1.00	1.00	0			1
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				152.00	59.90	25.93	1.00	1.00	1	Current sm	30	1
0		1	6	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	1	0				168.00	71.00	25.16	1.00	1.00	0			0
0		1	10	0	0	1	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	1	OSTEOART			154.00	63.00	26.56	1.00	1.00	0			0
0	0	0		0	0	0	0	0	0	0	1	0	0	0	0.00	1	0	1	0	0	0				161.00	67.00	25.85	1.00	1.00	1	Past smoke	40	0
0	0	0	6	0	1	1	0	0	0	0	1	0	0	0	0.00	0	1	0	0	1	0				180.00	95.00	29.32	1.00	1.00	1	Past smoke	10	1
0	0	1	6	0	0	1	1	0	0	0	0	0	0	0	0.00	0	1	0	1	0	0				158.00	75.30	30.16	2.00	1.00	1	Current sm	10	0
0		1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	1	0	1	0	0	0	OSTEOART			155.00	83.00	34.55	2.00	1.00	1	Current sm	7	1
0	0	1	6	0	0	1	1	0	0	0	0	0	0	0	0.00	0	1	0	1	0	0				158.00	84.50	33.85	2.00	1.00	1	Current sm	7	0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	1	0	0	1	OSTEOART			156.00	52.60	21.61	0.00	0.00	1	Past smoke	40	0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				168.00	60.80	21.54	0.00	0.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				152.00	51.00	22.07	0.00	0.00	1	Past smoke	40	0
0		1	1	0	0	1	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	1	OSTEOART			168.00	58.80	20.83	0.00	0.00	0			0
0	0	1	2	0	1	0	1	0	0	0	0	0	0	1	1.00	0	0	1	0	0	0				165.00	66.10	24.28	0.00	0.00	1	Current sm	40	0
0		1	25	0	1	0	1	0	0	0	0	0	1	1	1.00	0	0	0	0	0	0				162.00	56.00	21.34	0.00	0.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	1	0	1	OSTEOART			157.00	55.40	22.48	0.00	0.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				170.00	71.90	24.88	0.00	0.00	0			0
0		1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				168.00	63.50	22.50	0.00	0.00	1	Past smoke	8	1
0		1		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				172.00	61.00	20.62	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				163.00	78.00	29.36	1.00	1.00	1	Past smoke	5	1
0		1	8	0	1	1	1	0	0	0	0	0	0	0	0.00	0	1	1	0	0	0				161.00	65.00	25.08	1.00	1.00	1	Past smoke	50	0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	1	0	0	0				160.00	64.00	25.00	1.00	1.00	0			1
0		1	2	0	1	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				163.00	68.00	25.59	1.00	1.00	0			0
0		1	2	0	1	0	1	0	0	0	0	1	0	0	1.00	0	0	0	0	0	0				170.00	73.00	25.26	1.00	1.00	1	Past smoke	40	1
0	0	1	10	0	0	1	0	0	0	0	1	1	0	0	1.00	0	1	1	0	0	1	OSTEOART			163.00	82.00	30.86	2.00	1.00	1	Past smoke	12	1
0	0	1	5	0	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				163.00	117.50	44.22	2.00	1.00	0			1
0	1	1	16	0	1	0	1	0	0	0	1	1	0	1	1.00	0	1	1	0	0	1	OSA			165.00	97.00	35.63	2.00	1.00	1	Past smoke	25	1
0		1	2	0	1	0	1	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0				160.00	47.10	18.40	-1.00	0.00	1	Past smoke	40	0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	1	1	0	1	SCHIZOPHI			155.00	36.20	15.07	-1.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	1	0	0				160.00	45.90	17.93	-1.00	0.00	1	Current sm	40	0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				160.00	43.00	16.80	-1.00	0.00	0	Past smoke	10	0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				160.00	54.00	21.09	0.00	0.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				162.00	56.00	21.34	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				165.00	58.00	21.30	0.00	0.00	0			0
0	1	1	1	0	0	1	0	0	0	0	1	1	0	0	1.00	0	1	0	0	0	0				165.00	52.40	19.25	0.00	0.00	1	Past smoke	30	1
1		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				165.00	61.60	22.63	0.00	0.00	1	Past smoke	10	1
0		1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				162.00	58.00	22.10	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				187.00	69.00	19.73	0.00	0.00	1	Past smoke	30	0
0		1	1	0	1	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	1	OSTEOART			162.00	60.90	23.21	0.00	0.00	0			0
0	0	1	21	0	0	1	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				170.00	54.40	18.82	0.00	0.00	0			0
0		1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	1	0	0	0				177.00	66.30	21.16	0.00	0.00	1	Current sm	35	0
0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				155.00	58.00	24.14	0.00	0.00	1	Past smoke	20	1
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				163.00	60.10	22.62	0.00	0.00	0			0
0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	1	0	0	0				182.00	70.00	21.13	0.00	0.00	1	Past smoke	30	1
0		1	1	0	1	1	1	0	0	0	1	1	1	0	1.00	0	1	1	0	0	0				167.00	62.40	22.37	0.00	0.00	0	Past smoke	40	1
0	0	1	11	0	0	1	0	0	0	0	1	1	1	0	1.00	1	1	0	0	0	0				180.00	66.00	20.37	0.00	0.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				172.00	59.40	20.08	0.00	0.00	0			1
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				167.00	59.30	21.26	0.00	0.00	1	Current sm	40	0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	1	PERNICIOU			160.00	52.00	20.31	0.00	0.00	0			1
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	1	0	0	1				168.00	69.50	24.62	0.00	0.00	1	Past smoke	20	1
0		1	3	0	1	0	1	0	0	0	0	0	1	0	1.00	0	0	0	0	0	0				160.00	49.80	19.45	0.00	0.00	0			0
0	0	1	3	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				169.00	56.70	19.85	0.00	0.00	1	Past smoke	4	1
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	1	0	0	0				167.00	57.00	20.44	0.00	0.00	1	Past smoke	15	0
0	1	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				162.00	56.70	21.60	0.00	0.00	0			1
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				160.00	48.80	19.06	0.00	0.00	1	Past smoke	15	1
0	1	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				152.00	56.60	24.50	0.00	0.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0		0	0.00	0	0	0	0	0	0				168.00	62.80	22.25	0.00	0.00	0			0
0	0	1	9	1	0	0	1	0	0	0	0		0	0	0.00	0	0	0	0	0	0				164.00	59.60	22.16	0.00	0.00	1	Past smoke	20	0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				165.00	64.00	23.51	0.00	0.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0	0	1	1.00	0	0	1	0	0	0				175.00	65.30	21.32	0.00	0.00	1	Past smoke	5	0
0	0	1	3	0	0	1	1	0	0	0	0	0	1	0	1.00	0	1	0	0	0	0				157.00	57.00	23.12	0.00	0.00	0			0
0	0	1	6	0	1	0	1	0	0	0	1	1	0	0	1.00	0	0	1	0	0	0				152.00	53.40	23.11	0.00	0.00	0			0
0	0	1	2	0	0	0	1	0	0	0	1	1	1	0	1.00	0	1	1	0	0	0				166.00	65.00	23.59	0.00	0.00	1	Past smoke	35	1
0	0	1	11	0	1	0	1	1	0	0	1	1	1	0	1.00	0	0	0	0	0	0				180.00	73.00	22.53	0.00	0.00	0			0
0	0	0		0	0	0	0	0	0	0	0		0		0.00		0	1	1	0	0				167.00	65.00	23.31	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				166.00	55.50	20.14	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				170.00	72.20	24.98	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	1	OSTEOART			165.00	53.30	19.58	0.00	0.00	1	Current sm	20	0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				150.00	52.00	23.11	0.00	0.00	0			0
0	0	0	2	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				162.00	62.40	23.78	0.00	0.00	1	Past smoke	1	1
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	1	OSTEOART			165.00	66.00	24.24	0.00	0.00	0			1
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				152.00	51.00	22.07	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				170.00	72.00	24.91	0.00	0.00	1	Past smoke	30	1
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	1	0	0	0				160.00	54.70	21.37	0.00	0.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				167.00	57.20	20.51	0.00	0.00	1	Past smoke	15	1
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	1	1	0	0				157.00	61.00	24.75	0.00	0.00	0			0
0		1	3	0	1	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				157.48	54.00	21.77	0.00	0.00				1
0	0	1	21	0	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				171.00	63.70	21.78	0.00	0.00	0			0
0	0	1	3	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	1	OSTEOART			164.00	58.00	21.56	0.00	0.00	0			0
0	0	1	6	0	0	1	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				168.00	53.50	18.96	0.00	0.00	0			0
0	1	0		0	0	0	0	0	0	0	1	0	0	0	0.00	0	1	0	0	0	0				164.00	52.20	19.41	0.00	0.00	0			1
0	0	1	5	0	1	0	0	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0				158.00	61.00	24.44	0.00	0.00	0			0
0		1	28	0	1	1	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				172.00	85.00	28.73	1.00	1.00	0			0
0		1	12	1	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				168.00	71.40	25.30	1.00	1.00	0			0
0	0	1	2	0	1	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				169.00	81.00	28.36	1.00	1.00	0			1
0	0	1	11	0	1	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				167.00	79.00	28.33	1.00	1.00	1	Past smoke	10	1
0		1	7	0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				170.00	74.00	25.61	1.00	1.00	0			0
0	0	1	7	0	1	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				163.00	70.00	26.35	1.00	1.00	1	Past smoke	3	0
0		1		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				167.00	83.30	29.87	1.00	1.00	0			0
0	0	0		0	0	1	1	0	0	0	1	1	1	0	1.00	0	1	1	1	0	0	VITILIGO			168.00	71.80	25.44	1.00	1.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	1	0	0	0				158.00	64.70	25.92	1.00	1.00	0			0
0	0	1	3	0	1	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	1	OSTEOART			159.00	72.26	28.58	1.00	1.00	0			0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				161.00	69.00	26.62	1.00	1.00	0			0
0	1	1	5	1	0	0	0	0	0	0	1	1	0	0	1.00	0	1	0	0	0	0				167.00	78.00	27.97	1.00	1.00	0			1
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	1	0	0	0				180.00	86.00	26.54	1.00	1.00	0			0
0	0	1	6	1	0	1	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				160.00	67.00	26.17	1.00	1.00	0			0
0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	1	0	0	0				166.00	80.00	29.03	1.00	1.00	1	Past smoke	30	1
0		1		0	1	1	0	0	0	0	0	1	1	1	1.00	0	0	0	0	0	0				164.00	75.40	28.03	1.00	1.00	1	Past smoke	20	0
0	0	1	9	0	1	1	1	0	0	0	1	1	0	0	1.00	0	0	0	0	0	1	ATRIAL FIB			170.00	84.80	29.34	1.00	1.00	0			1
0	0	1	6	0	1	1	0	0	0	0	1	1	0	0	1.00	0	1	0	0	0	0				162.00	70.00	26.67	1.00	1.00	0			0
0	0	1	5	0	0	0	1	0	0	0	1	1	0	0	1.00	0	0	0	0	0	0				176.00	85.40	27.57	1.00	1.00	0			0
1	1	1	5	0	1	0	0	0	0	0	0	0	0	0	0.00	1	1	1	0	0	0				169.00	83.30	29.17	1.00	1.00	0			0
0	0	1	4	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				170.00	77.80	26.92	1.00	1.00	0			0
0	0	1	17	0	1	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				161.00	71.40	27.55	1.00	1.00	1	Past smoke	10	0
0		0		0	0	0	0	0	0	0	0	0	0	1	1.00	0	0	0	0	0	1	FILARIASIS			164.00	73.60	27.36	1.00	1.00	0			0
0	0	1		0	1	1	0	0	0	0	1	1	0	0	1.00	0	0	1	0	0	0				160.00	75.00	29.30	1.00	1.00	1	Past smoke	40	0
0	1	1	10	1	0	1	0	0	0	1	1	1	0	0	1.00	0	1	0	0	0	0				150.00	64.00	28.44	1.00	1.00	0			0
0	0	1	20	0	1	1	0	0	0	0	1	1	1	0	1.00	0	1	1	1	0	0				160.00	72.00	28.13	1.00	1.00	1	Past smoke	3	0
0	0	1	13	0	1	1	0	0	0	0	1	1	1	0	1.00	0	1	0	0	0	0				165.00	71.00	26.08	1.00	1.00	1	Past smoke	35	0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				165.00	71.80	26.37	1.00	1.00	0			0
0		1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				172.00	75.00	25.35	1.00	1.00	1	Current sm	30	1
0	0	1	2	0	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				156.00	65.00	26.71	1.00	1.00	0			0
0	1	1	20	1	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				168.00	72.00	25.51	1.00	1.00	1	Past smoke	20	0
0	0	1	20	1	0	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				158.00	73.90	29.60	1.00	1.00	0			0
0	0	1	2	0	1	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				160.00	67.00	26.17	1.00	1.00	0	Past smoke		1
0	0	1	12	0	0	1	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				164.00	69.80	25.95	1.00	1.00	0			0
0		1	1	0	1	0	1	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				172.00	81.00	27.38	1.00	1.00	1	Past smoke	4	1
0	0	1	10	0	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				160.00	67.00	26.17	1.00	1.00	0			0
0	1	0		0	0	0	0	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0				163.00	70.00	26.35	1.00	1.00	0			1
0		0		0	0	0	0	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0				172.00	82.00	27.72	1.00	1.00	0			0
0		1	1	0	0	1	1	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0				164.00	76.60	28.48	1.00	1.00	1	Past smoke	20	1
0		1	3	0	0	1	1	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0				169.00	83.00	29.06	1.00	1.00	1	Past smoke	50	1
0		1	1	0	0	0	1	0	0	0	1	0	0	0	0.00	1	1	0	0	0	0				175.00	77.00	25.14	1.00	1.00	0			0
0		1	6	0	1	0	1	1	0	0	0	0	0	0	0.00	0	1	0	0	0	0				158.00	77.90	31.20	2.00	1.00	0			1
0	0	1	20	0	1	0	1	0	0	0	1	1	0	0	1.00	0	1	0	0	0	0	OSTEOART			168.00	89.60	31.75	2.00	1.00	0			0
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	1	0	0	0				160.00	92.24	36.03	2.00	1.00	1	Past smoke	80	1
0	0	1	6	1	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				170.00	87.00	30.10	2.00	1.00	0			0
0	0	1	11	0	1	0	0	0	0	0	0	0	1	0	1.00	0	1	0	0	0	0				160.00	85.00	33.20	2.00	1.00	0			1
0	1	0	5	0	1	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				175.00	94.00	30.69	2.00	1.00	0			0
0		1	18	0	1	0	0	0	0	0	0	0	0	0	0.00	0	0	0	0	0	0				175.00	93.30	30.47	2.00	1.00	0			0
0	0	1	18	0	0	1	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				167.00	90.00	32.27	2.00	1.00	0			1
0	1	1	30	0	1	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				170.00	98.50	34.08	2.00	1.00	0			0
0		1	3	0	1	1	0	0	0	1	1	1	1	0	1.00	0	1	0	0	0	0				171.00	103.00	35.22	2.00	1.00	0			0
0	0	1	11	0	1	0	1	1	1	0	1	1	1	0	1.00	0	1	1	0	0	0				168.00	92.00	32.60	2.00	1.00	1	Past smoke	2	1
0	0	0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				165.00	92.80	34.09	2.00	1.00	1	Past smoke	3	0
0		0		0	0	0	0	0	0	0	0	0	0	0	0.00	0	0	1	0	0	0				158.00	76.00	30.44	2.00	1.00	1	Current sm	10	1
0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				162.00	86.00	32.77	2.00	1.00	0			0
1	0	1	15	0	0	1	1	0	1	0	0	0	0	0	0.00	0	1	0	0	0	0				163.00	83.00	31.24	2.00	1.00	0			0
0	0	1	11	1	0	0	1	0	0	0	0	0	0	0	0.00	0	1	0	0	0	0				162.00	80.00	30.48	2.00	1.00	0			0

Currentint	Durationin	TobaccoKh	N1Doyouh	N2Doyouh	N3Doyouh	N4Haveyou	N5Haveyou	N6Areyous	N7Areyour	N8Haveyou	N9Areyouf	N10Hasthe	ADAMtotal	adam17	ADAMfin	Weightloss	Exhaustion	Slowwalkir	Weakness	Decreased	FRIEDind	FRIEDfin	Weakness	Gripstreng	Standands	StandingFe	StandingSe	Standingfu	N3mwalkte	Totalscore	Haveyoufe	Doyouhave	walkingone
Past alcohc	25	1	1	1	1	0	1	1	1	1	0	1	8	1.00	1.00	1	1	1	1	1	5	1.00			13.7 – 16.6	1	1	No - 0	4.66 sec – (	<10	1	1	1
			1	1	1	0	0	0	1	1	1	1	7	1.00	1.00	1	1	1	1	1	5	1.00	14	12.0	13.7 – 16.6	1	1	>10 sec -2	3.62 -4.65 :	<10	1	1	1
Past alcohc	30	0	1	1	1	0	1	1	1	1	1	1	9	1.00	1.00	1	1	1	1	0	4	1.00	20	18.0	11.2 – 13.6	1	1	>10 sec -2	3.62 -4.65 :	>=10	1	1	1
Past alcohc	10	0	1	1	1	0	0	0	1	1	0	0	5	1.00	1.00	1	1	1	0	1	4	1.00			11.2 – 13.6	1	1	3-10 sec - 1	3.62 -4.65 :	<10	1	1	1
Past alcohc	30	0	1	1	1	0	1	1	1	1	0	1	8	1.00	1.00	1	1	1	0	1	4	1.00			13.7 – 16.6	1	1	>10 sec -2	4.66 sec – (	<10	1	1	1
Current alc	40	1	1	1	1	0	1	1	1	1	1	1	9	1.00	1.00	1	1	1	0	1	4	1.00			13.7 – 16.6	1	1	No - 0	4.66 sec – (	<10	1	1	1
Past alcohc	25		1	1	1	0	1	1	1	1	0	1	8	1.00	1.00	1	1	1	1	1	5	1.00	12	14.0	11.2 – 13.6	1	1	3-10 sec - 1	3.62 -4.65 :	<10	1	1	1
		0	1	1	0	0	0	0	1	1	1	1	6	1.00	1.00	0	1	1	1	1	4	1.00			>16,7 sec -	1	0	No - 0	>6.52 sec -	<10	1	1	1
		0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	1	1	1	1	4	1.00	16	15.0	>16,7 sec -	1	0	No - 0	3.62 -4.65 :	>=10	1	1	1
		0	1	0	0	0	1	1	1	0	0	1	5	1.00	1.00	1	1	1	0	1	4	1.00			11.2 – 13.6	1	1	>10 sec -2	4.66 sec – (	<10	1	1	1
		0	1	1	1	0	1	1	1	1	1	1	9	1.00	1.00	1	1	1	0	0	3	1.00			>16,7 sec -	1	1	No - 0	>6.52 sec -	>=10	1	1	1
Past alcohc	25	0	1	1	1	1	0	0	1	1	1	1	8	1.00	1.00	1	1	1	1	1	5	1.00	9	10.0	>16,7 sec -	0	0	No - 0	>6.52 sec -	<10	1	1	1
Current alc	30	0	1	1	1	0	1	1	1	1	0	1	8	1.00	1.00	1	1	1	0	1	4	1.00			13.7 – 16.6	1	1	>10 sec -2	4.66 sec – (	<10	1	1	1
		0	1	0	0	0	0	0	1	1	0	1	4	1.00	1.00	1	1	1	1	1	5	1.00	16	16.0	>16,7 sec -	1	1	>10 sec -2	4.66 sec – (	<10	1	1	1
		0	1	1	1	1	1	1	1	1	0	1	9	1.00	1.00	1	1	1	1	1	5	1.00			>16,7 sec -	1	0	No - 0	>6.52 sec -	<10	1	1	1
Past alcohc	10	0	1	0	1	0	1	1	1	1	0	1	7	1.00	1.00	0	1	1	0	1	3	1.00			13.7 – 16.6	0	0	No - 0	4.66 sec – (	<10	1	1	1
			1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	1	1	1	1	1	5	1.00	24	22.0	13.7 – 16.6	1	1	>10 sec -2	4.66 sec – (	<10	1	1	1
		0	1	1	0	0	1	1	1	0	0	1	6	1.00	1.00	1	1	1	1	1	5	1.00			13.7 – 16.6	1	1	No - 0	4.66 sec – (	<10	1	1	1
Past alcohc	20	0	1	0	1	0	1	1	1	0	0	0	5	1.00	1.00	0	1	1	0	1	3	1.00			11.2 – 13.6	1	1	>10 sec -2	>6.52 sec -	<10	1	1	1
		0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	1	1	1	0	3	1.00	27	7.8	13.7 – 16.6	1	1	No - 0	4.66 sec – (	<10	1	1	1
Past alcohc	30	0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	0	1	0	1	2	0.00	38	11.0	11.2 – 13.6	1	1		4.66 sec – (	<10	1	1	1
Current alc	30	0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	1	1	1	1	4	1.00	18	18.0	11.2 – 13.6	1	1	>10 sec -2	4.66 sec – (	<10	1	1	0
		1	1	1	1	0	1	1	1	1	0	1	8	1.00	1.00	0	1	1	1	1	4	1.00			>16,7 sec -	1	0	No - 0	>6.52 sec -	<10	1	1	1
		0	1	1	1	0	0	0	1	1	0	0	5	1.00	1.00	1	1	1	0	1	4	1.00			>16,7 sec -	1	0	No - 0	>6.52 sec -	>=10	1	1	0
		0	1	1	1	0	1	1	1	1	1	1	9	1.00	1.00	1	1	1	0	1	4	1.00			13.7 – 16.6	1	1	>10 sec -2	4.66 sec – (	<10	1	1	1
Past alcohc	20	0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	1	1	1	0	1	4	1.00			>16,7 sec -	1	0	No - 0	>6.52 sec -	<10	1	1	1
			1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	1	0	1	0	1	3	1.00			11.2 – 13.6	1	1	3-10 sec - 1	3.62 -4.65 :	<10	0	1	1
Current alc	30	1	1	1	1	0	1	1	1	1	1	1	9	1.00	1.00	0	1	1	0	1	3	1.00	30	24.0	11.2 – 13.6	1	1	>10 sec -2	>6.52 sec -	<10	1	1	1
		0	1	1	1	0	1	1	1	0	0	1	7	1.00	1.00	1	1	1	1	1	5	1.00	20	18.0	11.2 – 13.6	1	1	No - 0	3.62 -4.65 :	<10	1	1	1
		1	1	1	1	0	1	1	1	1	0	1	8	1.00	1.00	0	1	0	0	0	1	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
		1	0	0	0	0	0	0	0	0	1	0	1	0.00	0.00	1	0	0	1	0	2	0.00	18	22.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	1	0	0	0	0	1	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	0	0	1	0	0	1	0.00			<11.19.	1	1	>10 sec -2	3.62 -4.65 :	>=10	0	1	1
		0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	1	0	0	0	1	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
		0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			11.2 – 13.6	1	1	>10 sec -2	<3.62 sec -	>=10	0	1	0
		0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	1	0	0	0	1	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
		0	1	1	0	0	1	1	1	1	0	0	6	1.00	1.00	0	1	0	0	0	1	0.00			11.2 – 13.6	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
Past alcohc	8	0	1	1	1	0	0	0	1	0	0	1	5	1.00	1.00	0	1	0	0	0	1	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
		0	1	0	1	0	0	0	1	1	0	0	4	1.00	1.00	0	1	0	0	0	1	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
Past alcohc	15	0	1	0	0	0	1	1	0	1	1	1	6	1.00	1.00	0	1	0	0	0	1	0.00	30	28.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
Past alcohc		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	1	0	0	1	0	2	0.00	24	26.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	1	1	0	1	1	0	1	0	0	5	0.00	1.00	0	1	0	0	0	1	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
		0	1	1	1	0	1	1	1	1	0	1	8	1.00	1.00	0	1	0	0	0	1	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	1	0	0
Past alcohc	40	0	1	0	0	0	0	0	1	1	0	1	4	1.00	1.00	0	0	1	1	1	3	1.00	18	16.0	11.2 – 13.6	1	1	>10 sec -2	4.66 sec – 6.52 sec - 2		0	1	1
Past alcohc	15	0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			11.2 – 13.6	1	1	>10 sec -2	3.62 -4.65 :	>=10	0	1	0
Past alcohc	25	0	0	0	0	0	0	0	1	0	0	0	1	1.00	1.00	0	0	1	0	1	2	0.00			11.2 – 13.6	1	1	>10 sec -2	4.66 sec – (	<10	0	1	1
Past alcohc	25	0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	1	1	0	2	0.00	18	17.0	<11.19.	1	1	>10 sec -2	3.62 -4.65 :	>=10	0	1	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
			1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	1	1	1	0	0	0	1	1	1	1	7	1.00	1.00	0	0	0	1	0	1	0.00	11	14.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	30	0	0	0	0	0	0	0	1	0	0	0	1	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	5	0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	1	0	0	0	0	0	0	0	0	0	1	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	20	0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	30	1	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	40	0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	>6.52 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	3.62 -4.65 :	>=10	0	0	0
Current alc	30	0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	0	0	1	0	1	0.00	20	22.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00	28	30.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	30	1	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	1	0	1	0.00	18	15.0	<11.19.	1	1	3-10 sec - 1	<3.62 sec -	>=10	0	0	0
Past alcohc	10	0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	>6.52 sec -	>=10	0	0	0
Past alcohc	5		1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	1	0	1	0.00	20	20.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	30	1	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	>6.52 sec -	>=10	0	0	0
Past alcohc	15	0	0	0	0	0	0	0	1	0	0	0	1	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	1	0	1	0.00	21	12.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
			0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	1	0	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	35	0	1	0	1	0	0	0	1	1	0	1	5	1.00	1.00	0	0	0	1	0	1	0.00	24	20.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			11.2 – 13.6	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	35	0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	30	0	1	1	0	0	0	0	1	0	1	0	4	1.00	1.00	0	0	0	0	0	0	0.00	30	30.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	10	0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	30		1	0	1	0	1	1	1	1	0	1	7	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	25	0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00	30	28.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	1	1	0	0	0	0	1	0	1	4	0.00	1.00	0	1	0	1	0	2	0.00	24	24.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	30	1	0	0	0	0	0	0	1	0	0	0	1	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
			1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	1	0	1	0.00	26	27.0	<11.19.	1	1	>10 sec -2	<3.62 sec - 4		0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	10	0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	1	0	0	0	0	0	1	0	1	1	4	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	1	1	0	0	0	0	1	0	0	3	0.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	10	1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	15	0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	4	0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	1	0	1	0.00	20	17.0	<11.19.	1	0	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	1	1	0	0	0	1	0	0	0	4	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	1	0	0	0	1	1.00	1.00	0	0	0	1	0	1	0.00	26	21.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	1	0	1	0.00	15	18.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	30	1	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	1	0	0	0	0	1	1	0	1	5	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	30	1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	1	0	1	0.00	26	26.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	20	0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	3.62 -4.65 :	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	1	0	0	1	0.00			<11.19.	1	1	>10 sec -2	3.62 -4.65 sec -3		0	0	0
		0	0	0	0	0	1	1	1	0	0	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	1	0	1	0.00	10	11.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	30	0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	1	0	1	4	1.00	1.00	0	0	1	1	0	2	0.00	12	11.0	>16,7 sec -	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	30	0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	1	0	1	0.00	19	20.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	3.62 -4.65 :	>=10	0	0	0
Past alcohc	10	0	0	0	0	0	0	0	1	0	0	0	1	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	20	0	1	0	0	0	0	0	0	0	0	0	1	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	10	0	1	1	1	0	0	0	1	1	0	1	6	1.00	1.00	0	0	1	0	0	1	0.00			<11.19.	1	1	>10 sec -2	3.62 -4.65 :	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	20	1	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	>6.52 sec -	>=10	0	0	0
Past alcohc	10	0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00	36	36.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	1	1	1	0	0	0	4	1.00	1.00	0	0	0	1	0	1	0.00	25	22.0	<11.19.	1	1	3-10 sec - 1	<3.62 sec -	>=10	0	0	0
Current alc	35	0	0	0	0	0	0	0	1	0	1	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	20	0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00	28	29.0	<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Current alc	30	1	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
			1	1	1	0	0	0	1	1	1	1	7	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	25	0	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	0	0	0	0	0	0	1	0	1	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	0	0	0	0	0	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	4		0	0	0	0	0	0	1	0	0	0	1	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	0	1	0	0	0	1	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
Past alcohc	20		1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	0	0	0	0	0	1	0	0	1	0	2	0.00	0.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		0	1	0	0	0	0	0	1	0	0	0	2	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0
		1	1	0	0	0	0	0	1	0	1	0	3	1.00	1.00	0	0	0	0	0	0	0.00			<11.19.	1	1	>10 sec -2	<3.62 sec -	>=10	0	0	0

Doyouhave	Haveyoulo	FrailScale	Frailscalefi	FRAil	RObust	Weightloss	Inabilitytor	Doyounotf	SOF	SOFfin	Bioavailabl	UniqueKey	RecStatus	FKEY	GlobalReco	hypocomb	Osteoneck	NECKostec	NECKporo	osteoL1	LIosteo	L1poropen	osteoradiu	Radosteo	Radporope	Poropenia	Osteocoml	filter_$
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	87.1	118	1		03a714aa-	0	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	62.8	51	1		7476989f-	1												
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	126.0	38	1		9ad8142b-	1	2.00	1.00	1.00	2.00	1.00	1.00	2.00	1.00	1.00	1.00	1.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	105.0	6	1		fbfa2c8c-0	0	2.00	1.00	1.00	1.00	0.00	1.00	2.00	1.00	1.00	1.00	1.00	1
0	1	4	1.00	1.00	0.00	1	0	1	2.00	1.00	109.0	4	1		f1c37986-2	0	1.00	0.00	1.00	0.00	0.00	0.00	2.00	1.00	1.00	1.00	1.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	112.0	77	1		da57ff16-f	0	2.00	1.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	1.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	146.0	40	1		8b215729-	0	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	3	1.00	1.00	0.00	0	1	1	2.00	1.00	131.0	55	1		6a47a7b0-	1	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	3	1.00	1.00	0.00	0	1	1	2.00	1.00	44.6	157	1		d934fe14-2	1	2.00	1.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	1.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	116.0	97	1		4c77a27a-f	1	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	92.1	82	1		d840f6ec-4	0	1.00	0.00	1.00	2.00	1.00	1.00	0.00	0.00	0.00	1.00	1.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	32.4	56	1		288168bd-	1												
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00		81	1		9ee9df72-3	0												
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	71.9	66	1		fa2b9821-8	0												
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	127.0	95	1		9d2978c1-	0												
0	0	3	1.00	1.00	0.00	1	1	1	3.00	1.00	144.0	75	1		a663e23f-e	1												
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	34.8	119	1		1d413068-	1	1.00	0.00	1.00	0.00	0.00	0.00	2.00	1.00	1.00	1.00	1.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	171.0	22	1		32920861-	0	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1
0	0	3	1.00	1.00	0.00	0	1	1	2.00	1.00	69.0	98	1		72329fb2-a	1												
0	0	3	1.00	1.00	0.00	0	1	1	2.00	1.00	46.7	74	1		463be2b0-	1												
0	0	3	1.00	1.00	0.00	0	1	1	2.00	1.00	115.0	41	1		bfb5a2eb-	1												
0	1	3	1.00	1.00	0.00	0	1	1	2.00	1.00	79.2	108	1		6e6a0740-	1												
0	0	3	1.00	1.00	0.00	0	1	1	2.00	1.00	95.2	1	1		ff0ff4e1-87	1												
0	1	3	1.00	1.00	0.00	1	1	1	3.00	1.00	16.9	132	1		cec8ef91-1	1												
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	13.0	138	1		4975eb5c-	1												
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	67.1	10	1		fc32a1cb-1	1												
0	1	3	1.00	1.00	0.00	1	1	0	2.00	1.00	80.2	8	1		0f45752c-a	1	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	3	1.00	1.00	0.00	0	1	1	2.00	1.00	112.0	76	1		7293741e-	1	0.00	0.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	1	4	1.00	1.00	0.00	1	1	1	3.00	1.00	88.9	46	1		61d0b3ca-	1												
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	140.0	122	1		d5d7b826-	0	2.00	1.00	1.00	2.00	1.00	1.00	2.00	1.00	1.00	1.00	1.00	1
0	1	1	0.00	0.00	0.00	1	0	0	1.00	0.00	213.0	70	1		2bf0e75f-5	0	1.00	0.00	1.00	2.00	1.00	1.00	1.00	0.00	1.00	1.00	1.00	1
0	1	1	0.00	0.00	0.00	1	0	0	1.00	0.00	87.4	21	1		991ddc6b-	1	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	2	0.00	0.00	0.00	0	0	1	1.00	0.00	186.0	85	1		9a69bb58-	0	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	184.0	83	1		0ea1036c-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	37.0	120	1		800548a8-	0												
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	188.0	131	1		803ba63c-	0												
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	127.0	129	1		3eed4d56-	0												
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	71.0	93	1		d74825f2-l	1												
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	140.0	159	1		fc25ab10-7	0												
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	134.0	49	1		cf2c7279-7	0	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	1	1	0.00	0.00	0.00	1	0	0	1.00	0.00	93.3	39	1		4b84f58f-1	1	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	126.0	130	1		fc5d9383-3	0	1.00	0.00	1.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	157.0	123	1		46c5892b-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	2	0.00	0.00	0.00	0	1	1	2.00	1.00	103.0	72	1		a0476d0e-	0												
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	91.1	68	1		9d8f54b6-	1	0.00	0.00	0.00	0.00	0.00	0.00	2.00	1.00	1.00	1.00	1.00	1
0	0	2	0.00	0.00	0.00	0	1	1	2.00	1.00	61.1	128	1		956c5233-	1	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	1	0.00	0.00	0.00	0	0	1	1.00	0.00	80.3	69	1		5ff96ab0-5	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	169.0	156	1		92f30990-8	0	1.00	0.00	1.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	89.2	146	1		0eebaa7a-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	150.0	23	1		dc2297c5-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	151.0	11	1		dae73ae3-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	35.2	162	1		99eaffc3-5	0	2.00	1.00	1.00	2.00	1.00	1.00	2.00	1.00	1.00	1.00	1.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	236.0	111	1		5a3bf865-	0	2.00	1.00	1.00	2.00	1.00	1.00	2.00	1.00	1.00	1.00	1.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	116.0	58	1		0585581d-	0	1.00	0.00	1.00	1.00	0.00	1.00	2.00	1.00	1.00	1.00	1.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	273.0	103	1		ad7beb7a-	0	1.00	0.00	1.00	2.00	1.00	1.00	1.00	0.00	1.00	1.00	1.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	94.3	89	1		f54c1bca-0	1	1.00	0.00	1.00	2.00	1.00	1.00	1.00	0.00	1.00	1.00	1.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	122.0	29	1		1cead47f-1	0	1.00	0.00	1.00	2.00	1.00	1.00	1.00	0.00	1.00	1.00	1.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	94.7	18	1		8db0417a-	1	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	105.0	155	1		5468fffb-5	1	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	79.0	112	1		7444b74f-	0	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	133.0	79	1		d080fe4d-	0	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	153.0	14	1		192f3c46-7	0	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	35.2	161	1		9fdd4bd3-	1	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	118.0	151	1		065b58ea-	0	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	111.0	144	1		16855dda-	1	1.00	0.00	1.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	98.7	31	1		b05a8bf4-	0	1.00	0.00	1.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	103.0	37	1		a8020e75-	1	1.00	0.00	1.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	109.0	71	1		81809c08-	0	1.00	0.00	1.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	64.9	54	1		811c64bf-	1	0.00	0.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	129.0	26	1		9f5daafa-f	1	0.00	0.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	190.0	139	1		d0af22c1-b	0	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	64.5	36	1		8fa1e524-1	1	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	100.0	50	1		dc5bda7f-	1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	116.0	143	1		85cced03-	1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	170.0	124	1		b728e5b0-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	134.0	135	1		91f91cf3-c	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	148.0	115	1		926403ac-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	132.0	90	1		3af7dd90-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	151.0	43	1		3946f503-b	0	1.00	0.00	1.00							1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	108.0	140	1		18563f4f-1	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	95.2	2	1		64f536f8-2	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	120.0	35	1		771538b1-	0												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	81.3	52	1		f1bcb97f-9	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	139.0	110	1		bd964fff-d	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	143.0	117	1		8b77628d-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	106.0	153	1		2d0f43a2-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	73.9	25	1		bd118b15-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	113.0	78	1		32eb0269-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	121.0	28	1		b742f402-l	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	93.8	42	1		73c49ee4-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	86.8	5	1		46e19b92-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	141.0	109	1		2309a2e0-	0												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	145.0	16	1		63903d88-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	184.0	145	1		ea29ae29-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	118.0	44	1		ccbbbe80-	0												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	132.0	65	1		5ef89ab8-7	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	121.0	127	1		7cf63350-3	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	84.8	116	1		ddca4b71-	1												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	121.0	47	1		ad999f0f-e	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	91.7	9	1		37062fc7-c	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	158.0	141	1		f9b31147-l	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	167.0	150	1		94f0a0fd-9	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	61.6	147	1		5451d798-	0	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	109.0	92	1		ad4675e7-	1	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	93.8	114	1		5e4a1b52-	0	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	102.0	19	1		388c651a-	0	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	150.0	102	1		b633c518-	0	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	72.4	53	1		f8d5a0ff-e	0	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	178.0	86	1		69e4be37-	0	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	106.0	91	1		127ca7f7-3	0	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	116.0	96	1		62f8a784-7	0	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	146.0	63	1		aa5bf676-a	1	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	88.9	45	1		f4e2d261-l	0	1.00	0.00	1.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	118.0	94	1		7ada86d0-	1	0.00	0.00	0.00	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	129.0	107	1		6e854e99-	0	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	59.4	17	1		5ed63b5b-	1	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	85.2	73	1		e9c683e9-	0	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	153.0	134	1		4a3fb34b-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	81.3	30	1		82f6005e-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	94.7	32	1		41aedcac-l	1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	108.0	12	1		817c313a-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	101.0	67	1		b69d0b99-	1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	331.0	104	1		d5332e48-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	214.0	133	1		4838c08b-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	70.8	137	1		4cd602cd-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	66.1	121	1		b7791fd8-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	83.1	113	1		b953b3b3-	1												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	103.0	57	1		a10cb0d0-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	137.0	148	1		a18022dd-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	140.0	84	1		889960da-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	107.0	106	1		588aa55b-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	88.6	27	1		3867907c-	1												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	115.0	15	1		2277ee77-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	110.0	101	1		587b55b7-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	113.0	61	1		06cbbce0-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	90.9	7	1		f261e97c-a	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	164.0	149	1		835bff7a-6	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	134.0	136	1		3998f177-a	1												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	112.0	20	1		d5cc52e1-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	140.0	160	1		dd4ca5d3-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	106.0	142	1		543d37b1-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	127.0	62	1		17fbdbba-l	0												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	101.0	48	1		f9638820-f	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	131.0	87	1		0369c706-	0	1.00	0.00	1.00	2.00	1.00	1.00	2.00	1.00	1.00	1.00	1.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	72.2	60	1		8b50b2fc-	0	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	91.4	64	1		db12babb-	1	1.00	0.00	1.00	0.00	0.00	0.00	1.00	0.00	1.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	39.6	34	1		9d5d49b2-	1	1.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	157.0	126	1		3c297e48-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	107.0	13	1		b748df70-	1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	40.2	100	1		553fe254-	1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	599.0	88	1		bd2b8351-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	125.0	152	1		0ad9fcbc-e	1	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	81.9	158	1		1caec3ba-	0												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	85.9	59	1		93599665-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	125.0	154	1		c934c249-	0												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	126.0	24	1		3d95e973-	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00	105.0	80	1		f1162d02-	0												
0	0	0	-1.00	0.00	1.00	0	0	1	1.00	0.00	128.0	99	1		f3fd609a-d	1												
0	0	0	-1.00	0.00	1.00	0	0	0	0.00	0.00		33	1		d4382754-	1												