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Prevalence of Hypogonadism in Males of Different Age Groups: Is It A Lack of Awareness?

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ABSTRACT

Introduction: Hypogonadism in aging male is defined as "Syndrome caused by androgen deficiency which affect multiple organ functions and quality of life". Patients present with different symptoms like male erectile dysfunction, decreased sexual desire, anemia etc. **Objectives:** To demonstrate the serum testosterone levels and prevalence of hypogonadism in different age groups and their correlation with symptoms of hypogonadism. **Study Design:** Cross sectional comparative study. **Settings:** Allied Hospital Faisalabad. **Duration:** 3 years and 6 months, from Dec 1, 2015 to May 30, 2018. **Methodology:** 180 healthy looking males were randomly taken from attendants of patients of Urology Department from indoor or from OPD and categorized into six groups according to their age decades: starting from Group-I (20-29 years) and ending at Group 6 (70 years and above). Informed consent was taken. Symptoms of every person were recorded on Aging male symptoms scale (AMS) proforma/questionnaire. BMI, testicular volume, serum testosterone, Albumin, estradiol, SHBG, HbA1c and Blood Sugar were recorded. Results were recorded and put in SPSS version 10 for statistical analysis. **Results:** Average serum testosterone of different groups was 9.43±2.7ng/ml. The study shows a decrease in average serum testosterone level by 28.95% with advancing age. This difference is statistically not significant (chi square test, p-value 0.554). The prevalence of hypogonadism was 10% in advanced age groups of our study population and all persons having low testosterone were symptomatic. Study showed 93.44% increase in the severity of symptoms with advancing age. **Conclusion:** Serum testosterone falls with advancing age leading to different symptoms of hypogonadism but it is under reported as none of the persons was aware of this problem.

Keywords: Hypogonadism, Testosterone, Erectile dysfunction.

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INTRODUCTION

Hypogonadism in aging male is defined as "Syndrome caused by androgen deficiency which affect multiple organ functions and quality of life",[1] it may also be defined as "a syndrome caused by androgen deficiency and person having at least 3 sexual symptoms including low libido, impaired erections and decreased morning erections, decline in general wellbeing and fatique".[2,16]

Symptoms and signs of hypogonadism are decreased bone mineral density, decreased vigor, weakness, depressed mood, bone pains, decreased lean body mass, increased fat deposition, decreased muscle mass, decreased libido, decreased morning erections and male erectile dysfunction.[2,3] These symptoms and signs are also present in young men when their serum testosterone level decreases to below normal level and these symptoms reverse when androgen replacement therapy is started.[4,5] Hypogonadism in aging male has different synonyms: late onset hypogonadism (LOH),[6] androgen deficiency in aging male (ADAM), partial androgen deficiency in aging male (PADAM).[7]

Serum testosterone has got circadian rhythm due to pulsatile production of GnRH (Gonadotrophin releasing hormone) from the hypothalamus which acts on the pituitary to produce Gonadotrophin. Gonadotrophin acts on testes to produce testosterone.[8] Maximal level of testosterone is seen at 08:00 AM.[9] It starts declining at 10:00 AM and is minimal at 10:00 PM. So, to assess hypogonadism early morning sample should be taken.[10]

Hypogonadism may be primary or secondary or mixed. Primary hypogonadism is due to testicular failure to produce testosterone and laboratory findings show low serum testosterone and high serum FSH (Follicular Stimulating Hormone) & LH (Luteinizing Hormone) levels. In case of secondary hypogonadism serum testosterone, FSH & LH are all low as it is due to decreased production of Gonadotrophin from the pituitary gland. In mixed hypogonadism serum testosterone is low and serum FSH& LH are within normal limits. There is also a fourth variety of hypogonadism due to androgen insensitivity / resistance.[10]

Testosterone in blood is mostly (50-70%) protein bound, binding with sex hormone binding globulin (SHBH), 1-2% free and rest bound to serum albumin. Only free and albumin bound testosterone is bioavailable to tissues.

There is annual decrease in serum testosterone after the age of 40 by 0.5-2%.[11]

In aging male testosterone production is decreased by 20% in men aging > 60 years & by 30-40% in men aging >80years.[9,12] It is due to decreased Gonadotrophin production from decreased function of hypothalamus & pituitary glands and due to increased production of SHBG.[13] There is also increased conversion of testosterone to estradiol by aromatase enzyme. Hypogonadism leads to different complications like bone fracture, increased incidence of cardiovascular accidents, ischemic heart events, depressive mood and increased incidence of diabetes mellitus.[14,15]

These hormones are assessed in blood by different techniques like IRMA & Radioimmune assays etc. Different labs have different normal ranges but usually its range is from 300-1000 ng/dl.

In order to assess the hypogonadism, serum testosterone, serum albumin, LH, FSH, estradiol, Hb A_1C and SHBG all should be measured as all these affect the serum testosterone. In old age SHBG rises causing more testosterone to be in protein bound state and decreases free testosterone levels leading to hypogonadism. Similarly, FSH and LH are decreased in old age due to decreased production of GnRh from hypothalamus and ultimately decreased testosterone production. These gonadotrophins are also decreased in certain pituitary diseases. Serum albumin also bounds to testosterone but this testosterone is available to tissues. BMI and HbA1c are also measured as obesity increases estradiol levels and SHBG levels decrease in obesity and diabetes.

There are different incidences of hypogonadism in different decades of life ranging from 2.1% to 25% in different studies.[16,17] No study has been conducted in Pakistan on this LOH, so present study was conducted to assess the prevalence of hypogonadism in different age decades in Pakistani population and to see the correlation of symptoms of hypogonadism to serum testosterone levels.

Objectives:

1. To evaluate the prevalence of hypogonadism in aging male
2. To assess the symptoms of hypogonadism in different age group people
3. To correlate these symptoms with serum testosterone levels.

METHODOLOGY

Study design: Cross sectional comparative study.

Study setting: Allied Hospital Faisalabad

Duration of study: 3 years and 6 months, from Dec 01, 2015 to May 30, 2018.

Inclusion criteria: After approval from ethical committee a total of normal healthy looking male attendants of patients were taken from OPD Allied Hospital Faisalabad, attendants of patients in Urology Ward and willing workers among the employees of Allied Hospital Faisalabad. Six groups of people were made according to age decades: Group-I 20-29 years, group-II 30-39years, Group-III 40-49 years, Group-IV 50-59 years, Group-V 60-69years, Groups-VI 70 years and above.

- Informed consent was taken from all the patients.
- All the persons were given AMS (aging male scale) proforma to fill it. Uneducated persons and less educated persons were helped out in filling the proforma.
- Patient name, age, sex, height, weight and BMI were recorded.
- Testicular volume of every person was calculated by ultrasonography.
- Morning blood sample of every person was taken for serum testosterone, Serum FSH, Serum LH, SHBG, Serum Albumin, HbA1C and Random Blood Sugar.
- Blood sample were handed over to PINUM Laboratory for assessment of aforementioned tests.
- Results of tests were recorded on SPSS version 10.

Exclusion criteria:

- Person having any acute illness or chronic illness were excluded from study as these may affect serum testosterone levels.
- Persons taking certain medicines like steroids spironolactone, cimetidine, and any narcotic analgesic or alcohol users were also excluded from the study.

AMS Questionnaire

AMS Questionnaire

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."

Symptoms	Score = None 1	Mild 2	Moderate 3	Severe 4	Extremely severe 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, feeling fidgety)	☐	☐	☐	☐	☐
8. **Anxiety** (feeling panicky)	☐	☐	☐	☐	☐
9. **Physical exhaustion/lacking vitality** (general decrease in performance, reduced activity, lacking interest in leisure activities, feeling of getting less done, of achieving less, of having to force oneself to undertake activities)	☐	☐	☐	☐	☐
10. **Decrease in muscular strength** (feeling of weakness)	☐	☐	☐	☐	☐
11. **Depressive mood** (feeling down, sad, on the verge of tears, lack of drive, mood swings, feeling nothing is of any use)	☐	☐	☐	☐	☐
12. **Feeling that you have passed your peak**	☐	☐	☐	☐	☐
13. **Feeling burnt out, having hit rock-bottom**	☐	☐	☐	☐	☐
14. **Decrease in beard growth**	☐	☐	☐	☐	☐
15. **Decrease in ability/frequency to perform sexually**	☐	☐	☐	☐	☐
16. **Decrease in the number of morning erections**	☐	☐	☐	☐	☐
17. **Decrease in sexual desire/libido** (lacking pleasure in sex, lacking desire for sexual intercourse)	☐	☐	☐	☐	☐

Have you got any other major symptoms? Yes..... ☐ No..... ☐

If Yes, please describe: _____

Thank you very much for your cooperation

RESULTS

Group-I persons were having average BMI of 23.6 kg/m ^{2} and average testicular volume of 23.86 ml (ranging from 12.94 to 30.88 ml). Twenty-four persons (80%) were having no symptoms, 05 (16.66%) were having mild symptoms and only 01 (3.33%) had moderate symptoms score. Average serum

testosterone was 9.43±2.7ng/ml ranging from 1.89 to 16.20ng/ml. Average SHBG was 34.06nmol/L and serum estradiol was 36.67pg/ml. Serum albumin and HbA1c were normal in all patients. One patient was having decreased serum testosterone level of 1.89ng/ml and he was having testicular volume of 18ml and moderate symptoms score.

In Group-II fifteen (50%) persons had no symptoms, 12 (40%) had mild symptoms and 3 (10%) had moderate symptoms. Average BMI of this group was 26.13kg/m^2 and average testicular volume of 20.25ml (range 3ml to 30.67 ml). Average testosterone was 6.61±4.2ng/ml ranging from 2.02ng/ml to 18.27ng/ml. Five (16.67%) patients were having low serum testosterone. Among them 3 had moderate symptoms and 2 were having mild symptoms. Average of serum estradiol was 50.78 pg/ml and SHBG was 31.65 nmol/L. Serum albumin and HbA1c were normal in all patients.

In Group-III seventeen (56.66%) persons had no symptoms, 10 (33.33%) had mild symptoms and 3 (10%) had moderate symptoms. Average BMI of this group was 23.16kg/m^2 and average testicular volume of 21.35ml (rang 2.5ml to 33.5 ml). Average testosterone was 6.26±1.7ng/ml ranging from 3.03ng/ml to 42.37ng/ml. All patients were having normal serum testosterone. Average of serum estradiol was 54.60 pg/ml and SHBG was 35.33 nmol/L. Serum albumin was normal. HbA1c was raised in 01(3.33%) person and he was having moderate symptoms.

In Group-IV ten (33.33%) persons had no symptoms, 08 (26.66%) had mild symptoms, and 11 (36.66%) had moderate symptoms and only 01(3.33%) person had severe symptoms. Average BMI of this group was 22.53kg/m^2 and average testicular volume of 18.75ml (range17ml to 28.83ml). Average testosterone was 5.29±2.65 ng/ml ranging from 1.65 ng/ml to 11.13 ng/ml. Two (6.67%) patients were having low serum testosterone, 01(3.33%) was having moderate symptoms and other had severe symptoms. Average of serum estradiol was 62.15 pg/ml and SHBG was 41.7 nmol/L. Serum albumin was normal. HbA1c was raised in 01(3.33%) person and he was having moderate symptoms.

In Group-V thirteen (43.33%) persons had mild symptoms, 09 (30%) had moderate symptoms, 07 (23.33%) had severe symptoms and only 01 (3.33%) person had very severe symptoms. Average BMI of this group was 21.88kg/m^2 and average testicular volume of 19.94ml (range 6ml to 37.5ml). Average testosterone was 4.74±1.9 ng/ml ranging from 2.002 ng/ml to 9.06 ng/ml. Three (10%) persons were having low serum testosterone, 02 were having severe symptoms and 01 had very severe symptoms. Average of serum estradiol was 55.76 pg/ml and SHBG was 42.85 nmol/L. Serum albumin was normal. HbA1c was raised in 04 persons and all were having severe symptoms.

In Group-VI five (16.66%) persons had moderate symptoms, 12 (40%) had severe symptoms, and 03 (10%) had very severe symptoms. Average BMI of this group was 21.2kg/m^2 and average testicular volume of 18.53ml (range 7.28ml to 29.30ml). Average testosterone was 6.7±2.7 ng/ml ranging from 1.03ng/ml to 23.51ng/ml. Three (10%) persons were having low serum testosterone and all of them were having very severe symptoms and raised SHBG. Average of serum estradiol was 52.66 pg/ml and SHBG was 51.33 nmol/L. Serum albumin was low in 08 (26.67%) patients. HbA1c was raised in 04 (13.33%) persons and all were having severe symptoms.

There was average decrease of serum testosterone from 9.43 to 6.7ng/ml from group I to Group-VI which is 28.95% decrease from Group-I to Group-VI and by applying chisquare test this difference is insignificant (p-value 0.554).

The prevalence of hypogonadism was 3% in Group-I, 16.67% in group2, 0% in group 3, 6.67% in group4 and 10% in Group-V & VI.

There was 93.94% increase in severity of symptoms from Group I to VI.

The study shows a decrease in average serum testosterone level by 28.95% and a decline of 22.34% in average testicular volume with advancing age and 93.94% increase in the severity of AMS symptoms questionnaire with advancing age.

Table 1: Results of different tested parameters in all age groups

Groups	No. of Patients	Average BMI	Average Testosteron	Average Estradiol	Average SHBG	Average HbA1c	Average Albumin	Average Testicular Vol
		kg/m^2	ng/ml	pg/ml	nmol/L	%age	g/dL	ml
I (20-29)	31	23.6	9.43	36.67	34.06	5.02	4.54	23.86
II (30-39)	30	26.13	6.61	50.78	31.65	5.58	4.4	20.25
III (40-49)	40	23.16	6.26	54.60	35.33	6.02	4.38	21.35
IV (50-59)	37	22.53	5.29	62.51	41.7	5.75	4.20	18.75
V (60-69)	30	21.88	4.74	55.76	42.85	5.90	4.13	19.94
VI (~70)	34	21.2	6.7	52.66	51.33	5.87	3.72	18.53

Table 2: AMS symptom scores in different age groups

Age Groups	No Symptoms	Mild	Moderate	Severe	Bothersome
I (20-29)	24	05	01	-	-
II (30-39)	15	12	03	-	-
III (40-49)	17	10	03	-	-
IV (50-59)	10	08	11	01	-
V (60-69)	-	13	09	07	01
(70-Above)	-	-	15	12	03

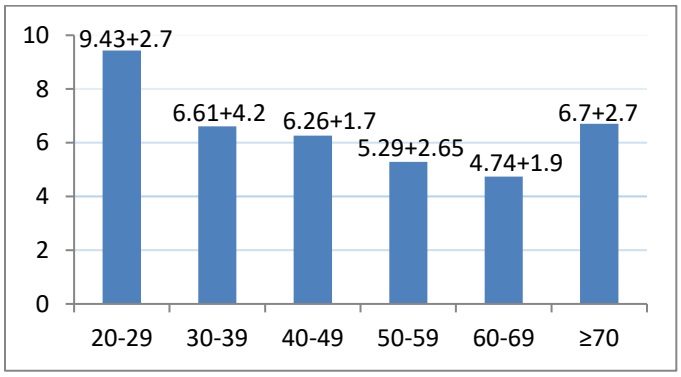

Figure 1: Serum testosterone levels (ng/ml) in different age groups

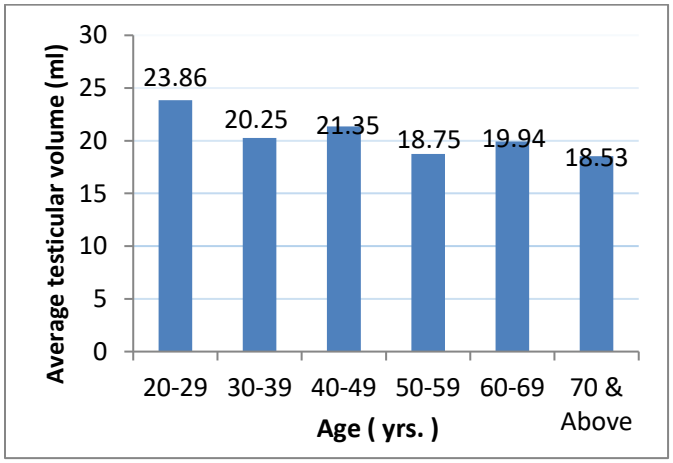

Figure 2: Average testicular volume (ml) in different age groups

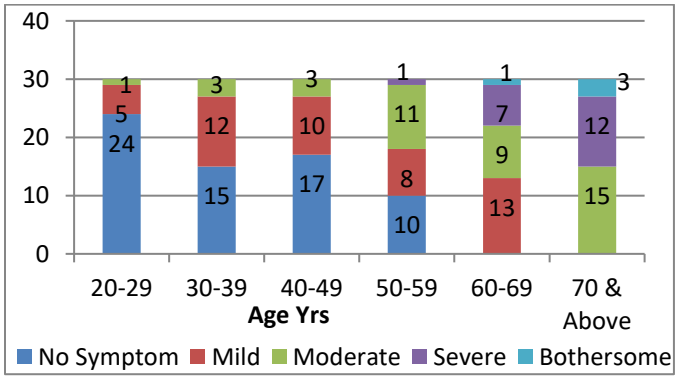

Figure 3: Correlation of severity of AMS with average serum testosterone levels in different age groups

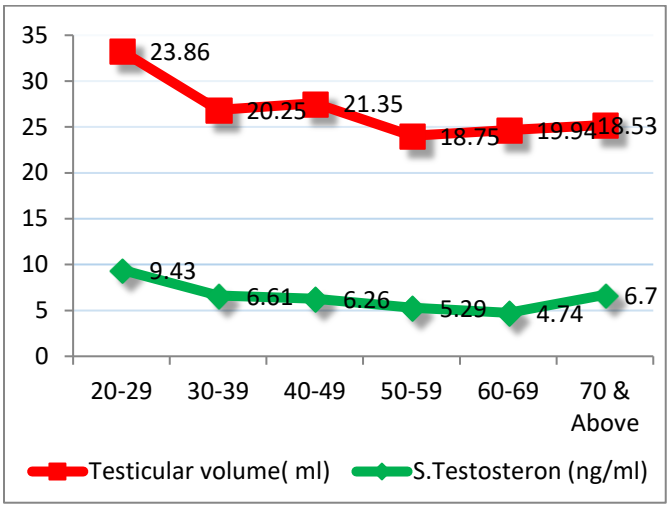

Figure 4: Correlation of serum testosterone and average testicular volume

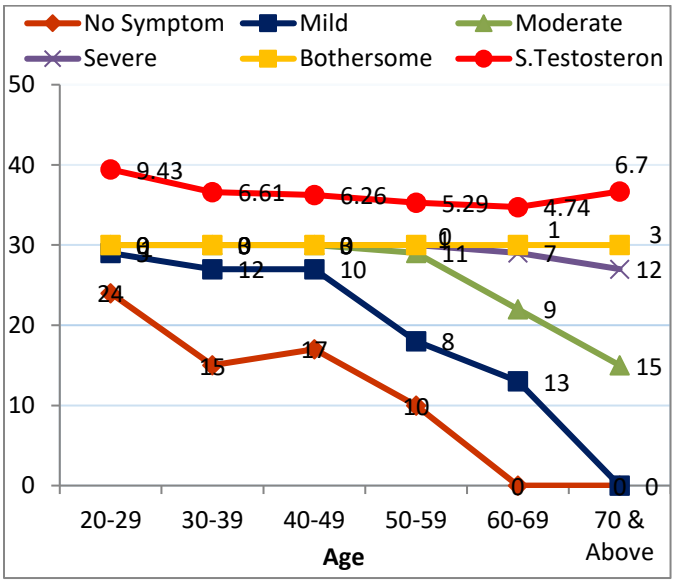

Figure 5: Severity of AMS symptom score in different age groups and its correlation with serum testosterone

DISCUSSION

Present study gives a glimpse of men's health in our study population which is taken randomly from people coming in Allied hospital Faisalabad Pakistan belonging to different races. Allied Hospital Faisalabad Pakistan has a very large catchment area comprising of many districts. Our study shows 28.29% decrease in serum testosterone level from group 1 to 6 but the symptoms score raised 93.94% which shows a disproportionate increase in severity of symptoms.

The EMAS study showed very low 2.1% overall prevalence of hypogonadism. Hypogonadism increases with age 0.1% (40-49 years), 0.6% in 50s, 3.2% in 60s and 5.1% in 70s.[16] In our study it is 6.67% in 50s and 10% in 60s & 70s.

In one study conducted by Prasanth et al the prevalence of hypogonadism was 20% in 60s and 50% in 80s.[17] while its 10%

in corresponding age groups in our study which is much less than Prasanth study.

In Baltimore study over all incidence of hypogonadism was 6-12.3%; 20% in 60s, 30% in 70s and 50% in 80s.[18] while in our study its 10% in 60s and 70s.

In Boston area study over all prevalence was 6.5%; 3.1-7.0% in less than 70 yeas age group, 18.4% in 70 years group.[19] It is 3-6.67% in < 70 yeas age groups and 10% in ≥ 70 years in our study.

A study conducted by Wang et al in China showed a prevalence of erectile dysfunction of 55.34 %, 88.2% and 91.7% in age groups 40-49, 50-59, 60-69 years respectively,[20] while in our study persons have 33.33%, 27.72% and 43.33% prevalence of erectile dysfunction in the corresponding age groups. In our study population persons in their late ages do not bother much about these symptoms as only one of our persons in group 5 had bothersome symptoms.

A study conducted by Kai Sun et al showed 59.88% prevalence of LOH using AMS Score[21] while in our study there is 65.96% prevalence of hypogonadism using AMS score. In Kai study the average testosterone of the people aging ≥ 40 years was 4.41ng/ml (15.284 nmol/liter) and in our study it is 5.83 ng/ ml. The decrease in testosterone is 24.28% when increasing age from 40 years to 60+ years while in Kai study this difference in testosterone was much less when age groups 40 years and above were taken; (15.047nmol/liter, 15.418 nmol/liter and 15.387nmol/liter for age groups ~40, ~50 and ~60 respectively). There is no difference in total testosterone levels in LOH positive and LOH negative persons.

CONCLUSION AND SUGGESTIONS

Serum testosterone falls with advancing age while our study subjects were not aware of it. It should be diagnosed and treated properly in elderly patients. Proper awareness campaigns should be started in this regard.

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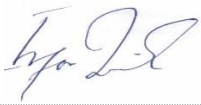
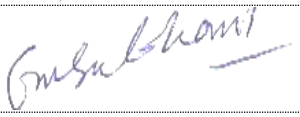
Dr. Muhammad Irfan Munir Assistant Professor, Urology FMU/Allied Hospital, Faisalabad	Write-up, Data collection, Manuscript preparation	
Dr. Ghulam Mahboob Subhani Associate Professor, Urology FMU/Allied Hospital, Faisalabad	Concept, Design, Definition of intellectual content, Data Collection	
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