Original Article

The Relationship between Low Testosterone Levels and Asthenia in Adult Patients

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Abstract

Objective: This study assesses the correlation between testosterone levels and fatigue severity, as measured by the NRS.

Methodology: This cross-sectional study was conducted from January to July 2024 at Hayatabad Medical Complex, Peshawar. A total of 150 adult patients presenting with asthenia were included. Serum testosterone levels were measured using standardized immunoassays. Fatigue severity was quantified using the Numeric rating scale (NRS), where patients rated their Fatigue on a scale from 0 (no fatigue) to 10 (extremely fatigued). Demographic data was summarized using descriptive statistics, while the Pearson correlation coefficient (r) was employed to evaluate the relationship between testosterone levels and fatigue severity.

Results: The frequency of low testosterone levels (<300 ng/dL) in the study was 40% (n=60). The average testosterone level for the low testosterone group was 250 ± 20 ng/dL, compared to 450 ± 30 ng/dL for those with normal testosterone levels. Patients with low testosterone had significantly higher Fatigue NRS scores (7.5 ± 1.5) than those with normal testosterone levels (3.2 ± 1.1) ($p < 0.001$). A significant negative correlation was observed between testosterone levels and fatigue NRS scores ($r = -0.65$, $p < 0.001$).

Conclusion: Low testosterone levels are prevalent in adult patients with asthenia and are significantly associated with increased fatigue severity, as measured by the NRS. These findings suggest that assessing testosterone levels in patients presenting with unexplained asthenia may be valuable, and testosterone replacement therapy could offer potential therapeutic benefits.

Keywords: Testosterone, Fatique, Numeric rating scale, Asthenia

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Introduction

Asthenia, or generalized weakness and Fatigue, is a common symptom in various medical conditions, particularly endocrine dysfunctions like hypogonadism.[1] Hypogonadism is diagnosed in men who have constantly documented low levels of testosterone on a fasting blood sample. If the levels are low on the initial screening, a repeat confirmation test is done on fasting as per guidelines. Testosterone replacement therapy (TRT) is recommended for patients with consistently low levels and who are symptomatic.

Testosterone is essential for muscle strength, energy regulation, and mood stabilization, and its deficiency (hypogonadism) has been associated with Fatigue and muscle weakness.[2] Previous studies on testosterone deficiency have focused primarily on middle-aged men.[3,4] Testosterone levels can significantly decrease with aging. Aging is also associated with sarcopenia, with a decrease in muscle mass, loss of energy, loss of libido, and osteoporosis. An increase in insulin resistance with aging can also increase adipose tissue deposition and lead to obesity. Symptoms of hypogonadism include asthenia, depression, mood changes, decrease in muscle mass, decreased libido, osteoporosis, and changes in hair and skin. It is also shown that testosterone treatment decreases insulin resistance and is also associated with lowering of BMI.[3,5] Centrally, the production of LH and FSH is decreased, while peripherally, they can impact Leydig and Sertoli cells and can also cause a decrease in the sex hormone binding globulin.[3]

Testosterone treatment is effective in decreasing symptoms of the patients and in correcting low testosterone levels.[4] Correction of testosterone levels can improve skeletal muscle mass and power, but it is not associated with reducing muscle fatigue.[6] This treatment has its limitations. It should be avoided in patients with prostate cancer and patients with a higher risk of cardiac and respiratory problems as it is associated with a greater incidence of adverse events related to the cardiac system, respiratory system, and skin. It is also associated with an increased prevalence of hypertension. The exact pathophysiology of the effect of testosterone treatment on the cardiovascular system is not clear and needs to be studied.[7] Current evidence suggests that TRT should be offered to patients with hypogonadism who are experiencing symptoms, as no long-term studies are looking at the effect of testosterone on the cardiovascular system and prostate.[8]

Testosterone, a key hormone in maintaining muscle strength, energy levels, and mood, is thought to play a significant role in managing asthenia. However, the relationship between low testosterone levels and asthenia, specifically quantified using the Numeric Rating Scale (NRS) for Fatigue, remains underexplored. This study assesses the correlation between testosterone levels and fatigue severity, as measured by the NRS.

Methodology

Study Design and Participants

We conducted a cross-sectional study involving 150 adult patients who presented with asthenia at Hayatabad Medical Complex, Peshawar, between January 2024 and July 2024. The inclusion criteria were adults aged 18 and older with a primary complaint of asthenia. Patients with known endocrine disorders other than testosterone deficiency and significant psychiatric conditions were excluded.

Data Collection

Participants underwent comprehensive clinical assessments, including a detailed medical history, physical examination, and laboratory tests. Serum testosterone levels were measured using standardized immunoassays. Fatigue was quantified using the Numeric Rating Scale (NRS). In this self-reported measure, patients rated their Fatigue on a scale from 0 to 10, with 0 representing "no fatigue" and 10 representing "worst fatigue imaginable."

Statistical Analysis

SPSS version 27 was used for statistical analysis. Descriptive statistics were used to summarize the demographic and clinical characteristics of the participants. Pearson's correlation coefficient was applied to examine the relationship between testosterone levels and fatigue severity, as measured by the NRS. A p-value of <0.05 was considered statistically significant.

Results

In our study, there were 150 male patients. The mean age of the patients was 45.2 ± 10.1 years, ranging from 18 to 67 years old (Figure 1). The average BMI of the patients was 26.8 ± 3.2 years. Forty-five patients (30%) of our study population had other comorbidities (Figure 2). The frequency of low testosterone levels (<300 ng/dL) in the study cohort was 40% (n=60). Patients with low testosterone levels had significantly higher Fatigue NRS scores compared to those with normal testosterone levels ($p < 0.001$). The mean Fatigue NRS score for low testosterone patients was 7.5 ± 1.5, while the mean Fatigue NRS score for normal testosterone was 3.2 ± 1.1 (Table 1). A significant negative correlation between testosterone levels and NRS scores ($r = -0.65$, $p < 0.001$) is observed. The r value shows that there is a strong negative correlation.

Discussion

The study demonstrates that low testosterone levels are highly prevalent among patients presenting with asthenia (generalized weakness and Fatigue) and are significantly associated with increased Fatigue on the NRS.[8-14] The negative correlation between testosterone

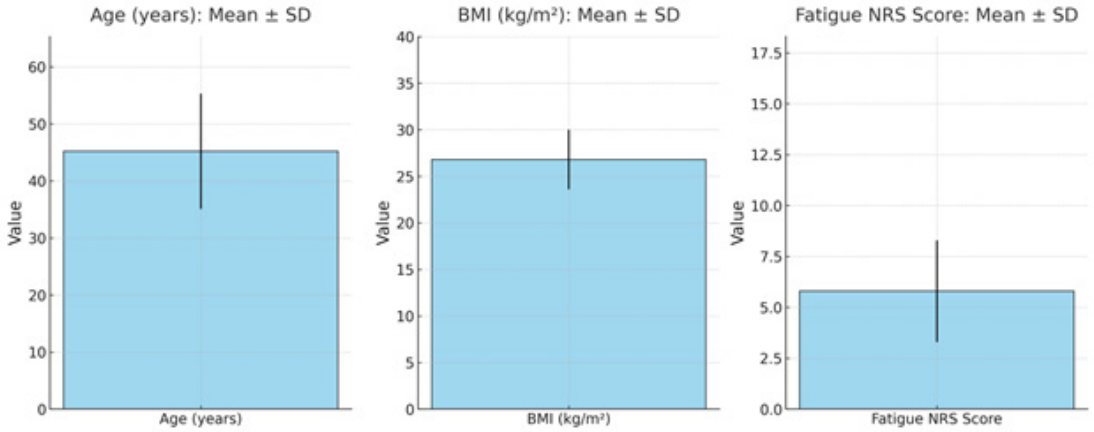

Figure 1: shows mean values for age, BMI, Fatigue, and standard deviation.

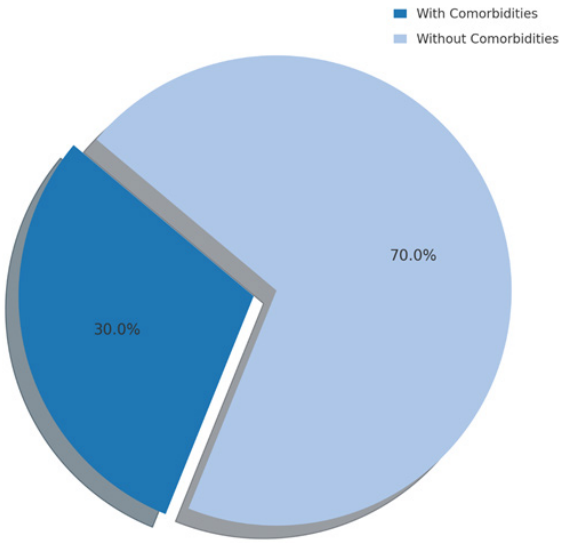

Figure 2: Showing the percentage of comorbidities in the study population

Table 1. Testosterone levels and Fatigue NRS scores

Testosterone Level	Fatigue NRS Score (Mean ± SD)	Number of Patients	P-value
Low (<300 ng/dL)	7.5 ± 1.5	60	<0.001
Normal (≥300 ng/dL)	3.2 ± 1.1	90	

levels and fatigue severity suggests that patients with lower testosterone experience higher levels of Fatigue. This finding is consistent with existing research, which has demonstrated a strong link between testosterone deficiency and both physical and mental Fatigue.[15,16]

Low testosterone, or hypogonadism, is a well-documented condition that becomes more prevalent with age, obesity, and certain chronic illnesses such as diabetes and cardiovascular disease. It can lead to a multitude of symptoms, including muscle weakness, reduced energy levels, decreased motivation, and depressive symptoms, which overlap with those of asthenia.[2,5,17] Testosterone plays an important role in maintaining muscle mass, energy metabolism, and mood stabilization, and its deficiency can profoundly impact a patient's ability to perform daily activities.[17]

Previous studies have consistently shown a positive effect of testosterone replacement therapy (TRT) in improving Fatigue, muscle strength, and mood in patients with documented testosterone deficiency.[16,17] Clinical trials have demonstrated that TRT can significantly improve both physical endurance and mental well-being,

making it a potential therapeutic strategy for patients experiencing asthenia due to low testosterone.[17] The association between low testosterone and increased Fatigue seen in this study further emphasizes the importance of considering testosterone deficiency in the differential diagnosis of patients presenting with unexplained Fatigue.

Clinical Implications

The findings of this study suggest several important clinical implications:

1. Routine Testosterone Screening in Fatigued Patients:

Patients presenting with asthenia that is unexplained should be investigated for low testosterone levels because of the strong association of hormone deficiency with fatigue.5, 12, 17 This is particularly relevant for patients who have other associated symptoms that point towards hypogonadism.

Screening should be mainly considered in middle-aged and older men, overweight individuals, and patients with chronic conditions like diabetes, metabolic syndrome, and chronic inflammatory diseases, where low testosterone levels are often prevalent.8,9

2. Potential for Testosterone Replacement Therapy (TRT):

If the patient presents with consistently documented low levels of testosterone, TRT can improve the patient's quality of life (QoL) by decreasing fatigue and improving muscle strength and libido.[15,16]

Patients should undergo thorough evaluation before initiating TRT as several conditions like cardiovascular diseases, hypertension, and prostate pathologies can be potentially impacted by this treatment. Monitoring the blood levels of testosterone and evaluating the patient for symptom improvement is essential to optimize the treatment.[17]

3. Comprehensive Patient Evaluation:

Other potential conditions that can cause asthenia should also be evaluated, such as thyroid dysfunction, sleep disorders, depression, and chronic pain syndromes. These conditions can masquerade as hypogonadism and should not be overlooked.[6,9]

In a nutshell, patient evaluation should be done properly before commencing TRT for patients with asthenia. At times, the etiology might be multifactorial.[13,18]

4. Further Research on Broader Populations:

Although our study shows a strong association of asthenia with T levels, further studies need to be done on other populations with larger sample sizes. The role of TRT needs to be explored in patients with other comorbidities as well.[18,19]

There is a need to conduct long-term studies to establish the safety and efficacy of this treatment as well.[20]

The limitations of this study are that it is a cross-sectional study and is unable to establish causality. Further work needs to be done in this regard and on larger populations to make the findings generalizable to the population.

Conclusion

Low testosterone levels are prevalent in adult patients with asthenia and are significantly associated with increased fatigue severity, as measured by the NRS. These findings suggest that assessing testosterone levels in patients presenting with unexplained asthenia may be valuable, and testosterone replacement therapy could offer potential therapeutic benefits.

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Authors' Contribution Statement

MI contributed to the conception, design, acquisition, analysis, interpretation of data, and drafting of the manuscript. IK contributed to the design, acquisition, analysis, drafting of the manuscript, and critical review of the manuscript. AJ contributed to the analysis, interpretation of data, critical review of the manuscript, and final approval of the version to be published. SJK contributed to the conception, interpretation of data, and final approval of the version to be published. All authors are accountable for their work and ensure the accuracy and integrity of the study

Confilct of Interest

Authors declared no conflict on interest

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None

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.