RESEARCH PAPER

Serum Testosterone Levels in Patients with Type 2 Diabetes Mellitus and Liver Dysfunction

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is commonly associated with hypogonadism and metabolic derangements. Liver dysfunction, frequently present in T2DM due to non-alcoholic fatty liver disease (NAFLD), may further impair testosterone metabolism, given the liver's role in sex hormone-binding globulin (SHBG) synthesis and steroid metabolism.

Aim: To evaluate serum testosterone levels in patients with type 2 diabetes mellitus and to assess their association with liver dysfunction.

Objectives: . 1. To estimate serum total and free testosterone levels in male patients with T2DM.

2. To assess liver function parameters in these patients.

3. To determine the association between testosterone levels, glycemic control (HbA1c), and liver dysfunction.

Materials and Methods: This cross-sectional study was conducted in the Department of General Medicine at Adichunchanagiri Hospital and Research Centre over 18 months. A total of 100 male T2DM patients aged 40–60 years were included. Clinical assessment, anthropometry, glycemic parameters (FBS, PPBS, HbA1c), liver function tests (LFT), renal parameters, and serum total and free testosterone levels were measured. Statistical analysis was performed using SPSS. A p-value <0.05 was considered significant.

Results: The mean total testosterone was 321.75 ± 180.67 ng/dL and free testosterone was 7.07 ± 3.96 pg/mL. Poor glycemic control (HbA1c >7%) was observed in 86% of patients. A significant proportion showed elevated liver enzymes suggestive of hepatic dysfunction. Testosterone levels were lower in patients with poor glycemic control and abnormal liver parameter

Conclusion: T2DM patients with liver function derangement exhibit significantly lower serum testosterone levels compared to those with normal liver function.

Keywords: Type 2 diabetes mellitus; liver dysfunction; serum testosterone; glycemic control; hypogonadism.

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance, relative insulin deficiency, and progressive β-cell dysfunction. It represents a major global health burden with rapidly increasing prevalence, particularly in developing countries like India. Beyond hyperglycemia, T2DM is associated with multiple endocrine and metabolic abnormalities, including disturbances in gonadal function. (7,8).

Hypogonadism is increasingly recognized as a common yet underdiagnosed comorbidity in men with T2DM. Approximately 30–50% of men with T2DM have subnormal testosterone levels. The pathophysiology is multifactorial and includes insulin resistance–mediated suppression of the hypothalamic–pituitary–gonadal (HPG) axis, increased visceral adiposity, chronic inflammation, and altered sex hormone-binding globulin (SHBG) synthesis. (1,2,5,9).

The liver plays a pivotal role in testosterone homeostasis. It is the primary site of:

- ***SHBG synthesis***
- ***Testosterone metabolism and clearance***
- ***Conversion of steroid hormones***

In patients with T2DM, non-alcoholic fatty liver disease (NAFLD) is highly prevalent, affecting nearly 60–70% of individuals. Hepatic steatosis and inflammation reduce SHBG production and impair androgen metabolism, thereby lowering circulating total testosterone levels. Additionally, hyperinsulinemia

suppresses hepatic SHBG synthesis, further contributing to reduced bioavailable testosterone.
Emerging evidence suggests a bidirectional relationship between testosterone deficiency and metabolic liver disease. Low testosterone promotes: (2,4,5).

- ***Visceral adiposity***
- ***Increased aromatase activity***
- ***Worsening insulin resistance***
- ***Hepatic fat accumulation***

Conversely, hepatic dysfunction exacerbates hypogonadism through impaired steroid metabolism. This metabolic–hepatic–endocrine interplay creates a vicious cycle that may accelerate disease progression and increase cardiovascular risk.
Despite growing evidence linking T2DM, liver dysfunction, and hypogonadism, data from the Indian population remain limited. Therefore, this study aims to evaluate serum total and free testosterone levels in male patients with T2DM and to assess their association with liver function derangement.

MATERIALS AND METHODS

In this study, 100 adult patients with Type-2 DM admitted to a tertiary care hospital were enrolled over an 18-month period
Study Design: Hospital-based cross-sectional study conducted over 18 months.
Sample Size: 100 patients (calculated using $n = Z^2pq/d^2$).
Inclusion Criteria: Male patients aged 40–60 years with T2DM.
Exclusion Criteria: Chronic liver disease of non-metabolic origin, alcohol use disorder, malignancy, and autoimmune disorders.
Investigations: HbA1c, LFT, total and free testosterone (morning sample).

Ethical considerations

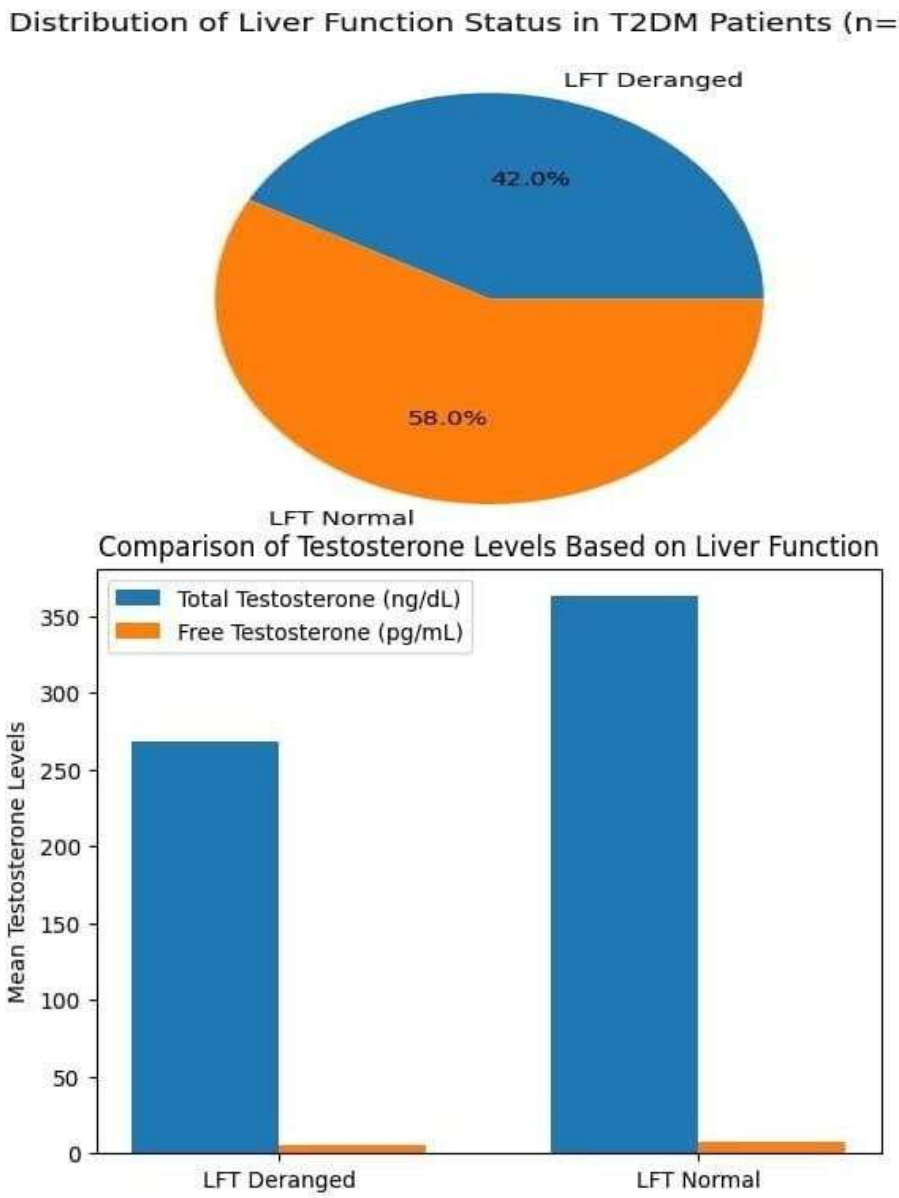
Institutional Ethics Committee approval was obtained prior to study initiation. Written informed consent was secured from all participants. Privacy and confidentiality were maintained.

RESULTS

PARAMETER	LFT DERRNGED(42)	LFT NORMAL(58)	P-VALUE
TOTAL TESTOSTERONE	268.4 ± 140.6	362.8 ± 192.3	0.02
FREE TESTOSTERONE	5.9 ± 3.1	7.9 ± 4.2	0.03

P value <.05 – statistically significant

Among the study population, 42% (n=42) had deranged liver function tests (ALT >40 U/L and/or AST >40 U/L)
Patients with elevated ALT had 25–30% lower mean testosterone levels compared to those with normal ALT levels



DISCUSSION

The present study demonstrates a statistically significant reduction in both total and free serum testosterone levels among male patients with Type 2 Diabetes Mellitus (T2DM) who exhibited deranged liver function tests compared to those with normal liver enzymes ($p = 0.02$ for total testosterone; $p = 0.03$ for free testosterone). The magnitude of difference observed (approximately 25–30% lower testosterone levels in the LFT-deranged group) is clinically meaningful and suggests a strong metabolic–hepatic contribution to androgen deficiency in this population.

Interpretation of Statistical Significance and Clinical Relevance

Although statistical significance was achieved, the clinical relevance deserves emphasis. A reduction of this magnitude in serum testosterone levels may shift patients from eugonadal to borderline or overt hypogonadal ranges, potentially influencing metabolic control, cardiovascular risk, and quality of life. Even modest reductions in testosterone have been associated with increased insulin resistance and adverse cardiometabolic outcomes in previous longitudinal studies.

Pathophysiological Integration

The relationship between T2DM, hepatic dysfunction, and hypogonadism is multifactorial:

1. Suppression of SHBG Synthesis:

The liver is the primary source of sex hormone-binding globulin (SHBG). Insulin resistance suppresses SHBG production, thereby reducing circulating total testosterone concentrations. Hepatic inflammation and steatosis further impair SHBG synthesis.

2. Central Hypogonadotropic Mechanism:

Chronic hyperinsulinemia and inflammatory cytokines suppress hypothalamic GnRH secretion, leading to reduced LH stimulation and impaired Leydig cell testosterone production.

3. Aromatization and Visceral Adiposity:

Excess visceral adiposity increases aromatase activity, converting testosterone to estradiol. Elevated estradiol exerts negative feedback on the hypothalamic–pituitary axis, worsening hypogonadism.

4. Hepatic Inflammation and Oxidative Stress:

NAFLD-associated inflammatory mediators and oxidative stress may directly impair steroidogenesis and alter hepatic androgen metabolism.

Bidirectional Relationship and Vicious Cycle

Importantly, testosterone deficiency itself promotes visceral adiposity, worsens insulin resistance, and may accelerate NAFLD progression. Thus, hepatic dysfunction both contributes to and is exacerbated by androgen deficiency, forming a self-perpetuating metabolic cycle.

Comparison with Existing Literature

Our findings are consistent with Dhindsa et al., who reported a high prevalence of hypogonadotropic hypogonadism in T2DM. Grossmann emphasized the cardiometabolic implications of low testosterone in diabetic men. Cheung et al. demonstrated that NAFLD independently predicts low testosterone levels. Yao et al. showed that reduced testosterone is associated with NAFLD progression.

Unlike prior studies primarily focusing on obesity or glycemic indices alone, the present study specifically demonstrates a statistically significant association between biochemical liver dysfunction and reduced testosterone levels in a defined hospital-based cohort.

Strengths

- ***Inclusion of both total and free testosterone measurements***
- ***Direct comparison between LFT-deranged and normal groups***
- Clearly defined inclusion and exclusion criteria • Statistically significant biochemical association

Limitations

- ***Cross-sectional design limits causal inference***
- ***Lack of SHBG measurement prevents assessment of binding protein contribution***
- ***No imaging confirmation of NAFLD severity***
- ***Single-center design with moderate sample size***
- ***Absence of multivariate regression analysis to adjust for confounders***

Future Directions

Future research should include:

- ***Prospective longitudinal designs***
- ***Measurement of SHBG, LH, FSH, estradiol***
- ***Imaging-based NAFLD grading***
- ***Multivariate regression analysis***
- Interventional trials assessing whether NAFLD treatment improves testosterone levels Clinical Implications

Routine evaluation of testosterone levels in T2DM patients with persistent liver enzyme elevation may allow early detection of hypogonadism. Integrated management focusing on weight reduction, glycemic optimization, and NAFLD treatment may potentially improve androgen status and metabolic outcomes.

Overall, the present study reinforces the concept that hepatic dysfunction significantly contributes to androgen deficiency in men with T2DM and highlights the need for integrated metabolic–endocrine evaluation. (1–6,9,10).

COMPARITIVE STUDIES

Present Study (2026)	**100 male T2DM patients (40–60 yrs)**	**Significantly lower total and free T in LFT-deranged group**	**Liver dysfunction significantly associated with reduced testosterone levels**
Author (Year)	Study Population	Key Findings	Conclusion
Dhindsaet al. (2004)	103 men with T2DM	High prevalence of hypogonadotropic hypogonadism	Low testosterone common in T2DM independent of age

Grossmann (2011)	Review of diabetic men	Association of low T with insulin resistance	Testosterone deficiency contributes to metabolic risk
Cheung et al. (2015)	Men with NAFLD	Lower T associated with hepatic steatosis	NAFLD independently predicts low testosterone
Yao et al. (2018)	Large cohort with T2DM	Low T linked to NAFLD progression	Testosterone deficiency worsens metabolic liver disease

CONCLUSION

T2DM patients with liver function derangement exhibit significantly lower serum testosterone levels, supporting the bidirectional metabolic–hepatic–endocrine relationship

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