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Original Article

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Pattern of Serum Testosterone Level in Kashmiri Men with Type 2 Diabetes Mellitus and its Correlation with Vitamin D Levels

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is increasingly prevalent in Kashmir, with significant metabolic and endocrine complications. Hypogonadism and vitamin D deficiency are emerging as important comorbidities that may worsen disease outcomes. ***Objective:*** To evaluate the pattern of serum testosterone levels in Kashmiri men with T2DM, estimate the prevalence of hypogonadism, and assess the correlation between testosterone and vitamin D levels. ***Methods:*** A cross-sectional observational study was conducted over 18 months at SMHS Hospital, Srinagar, including 250 Kashmiri men aged 20-59 years with T2DM. Clinical, biochemical, and hormonal parameters were assessed. Serum testosterone and 25-(OH)-vitamin D levels were analyzed in relation to age, BMI, and duration of diabetes. ***Results:*** Hypogonadism (testosterone <300 ng/dl) was detected in 39.2% of participants. Both testosterone and vitamin D levels showed significant age-related decline ($p<0.05$), with the lowest values in the 50-59 years group. Higher BMI and longer duration of T2DM were strongly associated with lower testosterone and vitamin D levels ($p<0.05$). Men with vitamin D sufficiency had higher mean testosterone compared to those with deficiency, indicating a positive correlation ($p=0.001$). No significant association was found between HbA1c and testosterone levels. ***Conclusion:*** Hypogonadism and vitamin D deficiency are highly prevalent in Kashmiri men with T2DM, particularly in obese individuals and those with long-standing diabetes. The positive correlation between vitamin D and testosterone highlights the importance of early hormonal screening and targeted interventions to reduce metabolic and cardiovascular risks in this population.

Keywords: ***Type 2 Diabetes Mellitus, Hypogonadism, Serum Testosterone, Vitamin D, Kashmir, Obesity, Duration of Diabetes***

Introduction

Diabetes mellitus (DM) represents a spectrum of chronic metabolic disorders marked by disturbances in carbohydrate, lipid, and protein metabolism, ultimately resulting in persistent hyperglycemia. The hallmark of DM is impaired glucose utilization by peripheral tissues and increased hepatic glucose production due to dysregulated gluconeogenesis and glycogenolysis, creating a state of metabolic imbalance [1]. Globally, diabetes has emerged as one of the most pressing public health challenges of the 21st century. Currently, an estimated 537 million adults live with the disease, a figure projected to escalate to 643 million by 2030 and 783 million by 2045 [2].

India bears a disproportionate burden of diabetes, ranking among the top countries with the highest prevalence. According to the World Health Organization, approximately 77 million Indian adults are currently affected by type 2 diabetes mellitus (T2DM), while an additional 25 million are classified as prediabetic [3]. Recent national surveys indicate geographical variability in prevalence, with southern states such as Kerala and Goa reporting rates as high as 4.1% [4]. The Kashmir valley, a region with unique dietary patterns and sociocultural factors, is witnessing an alarming rise in cases. Characterized by rice-based dietary habits and increasing urbanization, the region faces lifestyle-related risks that contribute significantly to the development of T2DM [5,6]. A survey conducted by the Indian Council of Medical Research (ICMR) confirmed a prevalence of 6.1% in Kashmir, underscoring the regional dimension of this epidemic [7].

The socioeconomic impact of diabetes is profound. In the United States, the annual expenditure associated with diagnosed diabetes was estimated at $413 billion in 2022, including $307 billion in direct healthcare costs alone [8]. Such figures highlight the immense strain diabetes places on both healthcare systems and individuals, particularly in low- and middle-income countries.

The diagnosis of diabetes is established through plasma glucose criteria, which include fasting plasma glucose ≥126 mg/dl, 2-hour plasma glucose ≥200 mg/dl during an oral glucose tolerance test (OGTT), or an HbA1C ≥6.5% [9]. In addition to genetic susceptibility, multiple modifiable factors have been implicated in

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the pathogenesis of T2DM. These include obesity, hypertension, central adiposity, physical inactivity, and unhealthy dietary patterns [10]. Good glycemic control remains the cornerstone of management and is strongly associated with a reduction in both microvascular and macrovascular complications. Early normalization of glycemia is known to reduce oxidative stress and prevent glycation of proteins and lipids, thereby delaying pathological processes driven by hyperglycemia [11].

Chronic hyperglycemia exerts deleterious effects on virtually every organ system. Long-term exposure accelerates the development of nephropathy, neuropathy, retinopathy, and cardiovascular disease [12-16]. Poorly controlled diabetes is also associated with immune dysfunction, oxidative damage, and accelerated atherosclerosis, thereby increasing the risk of coronary artery disease, stroke, and myocardial infarction [17,18]. Biochemically, these complications are mediated through mechanisms such as the formation of advanced glycation end products (AGEs), increased oxidative stress, and chronic low-grade inflammation. AGEs interact with their receptors (RAGE), inducing structural changes in basement membranes, altering vascular permeability, and promoting endothelial dysfunction [19,20]. Microvascular complications such as retinal lesions, microalbuminuria, and proteinuria are strong predictors of cardiovascular and cerebrovascular events in diabetic populations[22].

While hyperglycemia is the central driver of diabetic complications, emerging research suggests that hormonal imbalances also play an important role in the pathophysiology of T2DM. Of particular interest are testosterone and vitamin D, both of which have been implicated in glucose homeostasis, insulin resistance, and cardiovascular risk modulation.

Testosterone is the principal male sex hormone and anabolic steroid, exerting critical effects on the development of reproductive organs, muscle mass, bone density, and secondary sexual characteristics [23,24]. Beyond its reproductive functions, testosterone contributes to general health and well-being, influencing mood, cognition, and energy metabolism [25]. It is synthesized from cholesterol through multiple enzymatic steps and exerts its effects primarily via activation of the androgen receptor [26]. In men, the testes represent the main source of testosterone, while in women, the ovaries and adrenal glands contribute smaller amounts [27,28]. Serum testosterone concentrations in men are typically seven- to eight-fold higher than in women, with daily production rates approximately twenty times greater [29,30]. Normal serum levels in men range between 264 and 916 ng/dL, though these levels decline progressively with age [31-34]. By contrast, women typically exhibit mean concentrations of approximately 32.6 ng/dL, rising to 62.1 ng/dL in hyperandrogenic states [36,37].

A growing body of evidence links low serum testosterone to T2DM. Hypogonadism has been reported with high frequency in diabetic men [38-40], and inverse associations exist between testosterone levels and obesity, hypertension, dyslipidemia, and insulin resistance [41-45]. Furthermore, reduced testosterone has been associated with metabolic syndrome, increased cardiovascular morbidity, and premature mortality [46-52]. Recognizing this, the Endocrine Society's Clinical Practice Guideline (2010) recommended measuring serum testosterone in diabetic men presenting with symptoms of androgen deficiency such as sexual dysfunction, unexplained weight loss, or frailty [53]. Nevertheless, the utility of routine screening in asymptomatic individuals remains controversial, and ongoing trials continue to explore the potential benefits of testosterone replacement therapy in this population [54-56].

Parallel to testosterone, vitamin D has attracted significant interest in diabetes research. Once considered solely a regulator of calcium and phosphate homeostasis, vitamin D is now recognized as a multifunctional hormone with wide-ranging systemic effects. Vitamin D deficiency is a global concern affecting both developed and developing nations [57]. Its receptors are expressed in a variety of tissues, including skeletal muscle, cardiovascular, immune, and reproductive systems, suggesting broad physiological roles [58-62].

Vitamin D acts through genomic and non-genomic mechanisms, regulating nearly 3% of the human genome [63,64]. Importantly, vitamin D has been implicated in steroidogenesis, with evidence of vitamin D receptor (VDR) expression in Leydig and Sertoli cells, as well as germ cells and spermatozoa [65]. Experimental data suggest that calcitriol, the active form of vitamin D, may modulate luteinizing hormone (LH)-mediated steroidogenesis in Leydig cells through calcium-dependent pathways [66]. Its synthesis begins in the skin via UV light-driven conversion of 7-dehydrocholesterol, linking environmental factors such as sunlight exposure to endocrine regulation [67-69]. Beyond systemic effects, vitamin D exerts local paracrine and autocrine actions, which may be critical in modulating testicular function[70,71].

Collectively, these findings suggest potential interplay between vitamin D status, testosterone levels, and glucose metabolism. While the role of testosterone in male physiology is well established, vitamin D's influence on androgen production and its implications for T2DM remain less clear. Understanding this relationship may provide new therapeutic insights into the prevention and management of diabetes and its complications.

Aims and Objectives

- To assess pattern of testosterone levels in men with type 2 Diabetes Mellitus.
- To estimate prevalence of Hypogonadism in men with type 2 Diabetes Mellitus.
- To study correlation of serum testosterone level with Vitamin D levels.

Materials and Methods

Study Place: The study was conducted in the Postgraduate department of General Medicine, in collaboration with the Department of Biochemistry, at SMHS Hospital, an associated hospital of Government Medical College Srinagar.

Ethical Clearance: The study was reviewed and approved by the ethical committee of our institute.

Study Design: A cross sectional observational study was conducted from January 2022 to JULY 2023.

Study Period:18 months

Inclusion criteria

1. Men aged>20 and <60 years
2. All kashmiri men with Type 2 diabetes mellitus as per American Diabetes Association Standards of Medical Care in Diabetes (2021)
3. Duration of diabetes up to six months and above

Exclusion criteria

1. Men with type1 diabetes
2. Age<20and>60 years

3. Menonsteroid/and Rogen replacement/chemotherapeutic agents
4. Men with known hypergonadotropic hypogonadism
5. Men with known hypogonadotropic hypogonadism
6. All patients with comorbid condition like CLD/ CKD.

Assessment: After an overnight fast of 10 hours, a pooled venous blood sample will be drawn in the morning for investigations like complete hemogram, kidney and liver function, and fasting blood glucose, glycated hemoglobin and lipid profile. Serum will be separated within one hour, and preserved for estimation of serum testosterone, FSH, LH, Prolactin, and vitamin D. 27 Material and Methods

Outcomes: Various parameters will be recorded as per protocol which includes age, sex, anthropometry, symptoms and their duration. Physical examination findings including general physical examination for signs of insulin resistance and systemic examination will be recorded in the proforma. This will be followed by base line CBC, KFT, LFT, Lipid Profile, Thyroid Profile, Serum testosterone, FSH, LH, Prolactin, vitamin D. Subjects will be screened for complications of diabetes which included 24-hour urinary protein excretion and dilated fundus examination by an ophthalmologist.

Sample Size: The required Sample size was calculated using Open EPI software sample size calculator. At a 95% Confidence Interval and 80% Power considering a Standard Deviation of 1.3 and Mean difference of 0.8 for HBA1C, the required sample size came to be 250.

Statistical analysis: The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 26.0 (SPSS Inc., Chicago, Illinois, USA) and R software. Descriptive analysis for clinical, hormonal and biochemical parameters were preformed. Continuous variables were expressed as Mean± SD and categorical variables were summarized as frequencies and percentages. Graphically the data was presented by bar line diagrams and pie charts.A P-value of less than 0.05 was considered statistically significant.

Results

The age groups are divided into four categories: 20-29 years, 30-39 years, 40-49 years, and 50-59 years. Among the participants, 24 individuals (9.6%) fall within the 20-29 years age group, 52 individuals (20.8%) are in the 30-39 years age group, and 81 individuals (32.4%), are in the 50-59 years age group. The majority of participants, 93 individuals (37.2%) belong to the 40-49 years age group. The total number of participants is 250, representing 100% of the study sample. In the study population, 60 individuals (24 %) reported experiencing osmotic symptoms, while 40 individuals (16%) had weight loss. No participants (0.0%) exhibited ketosis. The majority of the participants, 150 individuals (60%), were diagnosed incidental.

To compare serum total testosterone among subjects, study participants were divided into four age groups: Group I (20-29 years, N=24), Group II (30-39 years, N=52), Group III (40-49 years, N=93), and Group IV (50-59 years, N=81). Serum total testosterone levels were highest in Group I (335±1.28 ng/dl) and decreased in the older age groups, with Group II at 295±1.02 ng/dl, Group III at 286±1.93 ng/dl, and Group IV at 260±1.23 ng/dl. This difference between the groups was statistically significant ($p<0.05$). This pattern suggests a potential age-related decline in testosterone levels among the study participants as depicted in table 1 below.

Table 1: Age-related decline in testosterone levels

Age (in Years)	N	Serum Testosterone (ng/dl) Mean ± SD	P-value
I-20-29	24	335±1.28	**0.024**
II-30-39	52	295±1.02	
III-40-49	93	286±1.93	
IV-50-59	81	260±1.23	

Vitamin D levels also showed a downward trend with age. Group I had the highest levels (36±2.31 ng/ml), significantly higher than other groups. Group II, Group III, and Group IV had mean Vitamin D levels of 20.29±9.24 ng/ml, 19.6±11.46 ng/ml, and 18.43±10.93 ng/ml, respectively. Notably, Group I's Vitamin D levels were significantly ($p<0.05$) higher compared to the older groups as shown in table 2 below.

Table 2: Age-related variation in vitamin D levels

Age (in Years)	N	Serum25-(OH)-Vitamin D (ng/ml) Mean ± SD	P-value
I-20-29	24	36±2.31	**0.001**
II-30-39	52	20.29±9.24	
III-40-49	93	19.6±11.46	
IV-50-59	81	18.43±10.93	

On investigating HbA1c levels among study participants categorized according to WHO BMI criteria into four groups: Group I (Underweight, BMI<18.5,N=20), Group II (Normal weight, BMI 18.5-24.9, N=180), Group III (Overweight, BMI25-29.9, N=30),and Group IV (Obese, BMI ≥30,N=20).The lowest HbA1c(%) levels were observed in Group I (7±0), with levels gradually increasing across the groups, peaking in the obese group (Group IV) at 9.95±2.17 as depicted in table 3. This difference between the groups was statistically significant ($p<0.05$).

Table 3: Age-related variation in HbA1c levels

WHOBMI (Kg/m^2)	N	HbA1c (%) Mean±SD	P-value
I-(<18.5)	20	7±1.22	**0.010**
II-(18.5-24.9)	180	7.74±1.31	
III-(25-29.9)	30	7.91±1.49	
IV-(≥30)	20	9.95±2.17	

On comparing serum testosterone levels among study participants categorized according to WHO BMI criteria into four groups: Group I (Underweight, BMI <18.5, N=20), Group II (Normal weight, BMI 18.5- 24.9,N=180), Group III (Overweight,BMI25-29.9,N=30), and Group IV (Obese, BMI ≥30, N=20).Testosterone (ng/dl) levels were significantly higher in Group I (320±5.17) and decreased further with increasing BMI, with Group IV showing the lowest levels among the overweight and obese categories(265±3.12).This difference between the groups was statistically significant ($p<0.05$), table 4 below.

Table 4: Relation of BMI with testosterone levels

WHO BMI(Kg/m^2)	N	Serum total testosterone (ng/dl) Mean±SD	P-value
I-(<18.5)	20	320±5.17	**0.001**
II-(18.5-24.9)	180	298±2.14	
III-(25-29.9)	30	285±4.23	
IV-(≥30)	20	265±3.12	

On comparing vitamin D levels among study participants categorized according to WHO BMI criteria into four groups: Group

I (Underweight, BMI<18.5, N=20), Group II (Normal weight, BMI 18.5-24.9, N=180), Group III (Overweight, BMI25-29.9, N=30), and Group IV (Obese, BMI≥30, N=20). The highest levels of 25-(OH)-Vitamin D (ng/ml) were found in Group I (38±5.17), with levels decreasing significantly ($p<0.05$) in the higher BMI groups, reaching the lowest in Group IV (16.26±9.06) as shown in table 5 below.

Table 5: Relation of BMI with vitamin D levels

WHOBMI (Kg/m^2)	N	Serum 25-(OH)-vitamin D(ng/ml) Mean±SD	P-value
I-(<18.5)	20	38±5.17	**0.001**
II-(18.5-24.9)	180	21.26±11.24	
III-(25-29.9)	30	18.59±11.03	
IV-(≥30)	20	16.26±9.06	

On comparing serum total testosterone among study participants categorized by the duration of T2DM into five groups: Group I (1-5years, N=47), Group II (6-10years, N=66), Group III (11-15years, N=50), Group IV (16-20 years, N=42), and Group V (21-25 years, N=45). The highest mean testosterone (ng/dl) level was observed in Group I (320±5.10ng/dl), suggesting that shorter durations of T2DM are associated with relatively higher testosterone levels. Testosterone levels declined with increasing duration of T2DM, with Group II showing 300±10.6 ng/ml, Group III at 290±9.15ng/ml, and GroupIVat270±4.32ng/ml. The lowest testosterone levels were seen in Group V (260±5.88 ng/ml), indicating a significant decrease in testosterone with prolonged diabetes duration. This difference between the groups was statistically significant ($p<0.05$), table 6 below.

Table 6: Relation of duration of T2DM with testosterone levels

Duration of T2DM (in years)	N	Serum total testosterone (ng/dl) Mean±SD	p-Value
I-(1-5)	47	320±5.10	**0.001**
II-(6-10)	66	300±10.6	
III-(11-15)	50	290±9.15	
IV-(16-20)	42	270±4.32	
V-(21-25)	45	260±5.88	

On comparing 25-(OH)-vitamin D levels among study participants categorized by the duration of T2DM into five groups: Group I (N=47), Group II (N=66), Group III (N=50), Group IV (N=42), and Group V (N=45). 25-(OH)-vitamin D (ng/ml) levels followed a downward trend with the increasing duration of T2DM. Group I had relatively high levels (24.83±10.01 ng/ml), which remained similar in Group II (24.94±10.68 ng/ml). However, a marked decrease was observed in Group III (19.58±5.47 ng/ml), Group IV (15.73±4.55 ng/ml), and Group V (13.3±2.29ng/ml), with the lowest levels recorded in those with the longest duration of diabetes(21-25years) as shown in table 7. The mean difference between the groups was statistically significant with p- value <0.05.

Table 7: Relation of duration of T2DM with vitamin D levels

Duration of T2DM (in years)	N	Serum25-(OH)-Vitamin D(ng/ml) Mean±SD	P-value
I-(1-5)	47	24.83±10.01	**0.001**
II-(6-10)	66	24.94±10.68	
III-(11-15)	50	19.58±5.47	
IV-(16-20)	42	15.73±4.55	
V-(21-25)	45	13.3±2.29	

The table 8 below shows the relationship between Vitamin D levels and serum testosterone levels in participants. It categorizes Vitamin D into four groups: <20 ng/ml, 20-29.9 ng/ml, 30-100 ng/ml, and >100 ng/ml. Mean testosterone levels increase with Vitamin D, from 280±5.09 ng/dl in the lowest group to 310±5.01 ng/dl in the highest. In other words patients with normal levels of vitaminD have normal testosterone level. A p-value of 0.001 indicates a significant difference across the categories.

Table 8: Relationship between Vitamin D levels and serum testosterone levels

Vitamin Dcategories (ng/ml)	N	Testosterone level (ng/dl)	P-value
(<20)	110	280±5.09	**0.001**
(≥20-29.9)	80	295±4.13	
(≥30-100)	60	310±5.01	
>100	0	0	

On comparing lipid parameters between participants, the mean serum total cholesterol (mg/dl) level were 205.29±57.3 in the low testosterone group, compared to 201.69±6.61 in the normal testosterone group with p-value of 0.822 indicating that the difference is not statistically significant. Participants with low testosterone had a mean triglyceride (mg/dl) level of 143.55±60.611, while those with normal testosterone had 120.92±49.98, with p-value of 0.202 indicating no statistically significant difference. The mean serum HDL cholesterol level (mg/dl) was lower in the low testosterone group30.39±7.96 compared to the normal testosterone group (41.08±11.96) with p-value of 0.056 indicating no statistical significance. The mean LDL cholesterol (mg/dl) level was 100±30.74 in the low testosterone group and 71.85±25.77mg/dl in the normal testosterone group with p-value of 0.463 shows the difference between the two groups is not statistically significant as shown in table 9 below.

Table 9: Comparing lipid parameters between participants

Parameter	Low Testosterone <300 (ng/dl) (Mean±SD) N=98	Normal Testosterone ≥300 (ng/dl) (Mean±SD) N=152	p-Value
Serum total cholesterol (mg/dl)	205.29±57.3	201.69±6.61	0.822
Serum triglyceride (mg/dl)	143.55±60.61	120.92±49.98	0.202
Serum HDL (mg/dl)	30.39±7.96	41.08±11.96	0.056
Serum LDL (mg/dl)	100±30.74	71.85±25.77	0.463

In this study, the prevalence of hypogonadism based on low serum testosterone levels (<300 ng/dl) among Kashmiri men with Type 2 Diabetes Mellitus (T2DM) was found to be 39.2 which is significantly high. Out of the total 250 participants, 98 exhibited testosterone levels below the normal reference range as depicted in table 10 below.

Table 10: Prevalence of hypogonadism among participants

Hypogonadism status	Frequency(N)	Percentage (%)
Yes	98	39.2
No	152	60.8

Discussion

In this study age distribution showed that the largest proportion of participants were middle-aged, consistent with global patterns of T2DM prevalence. Mathur *et al*. (2022) reported that the highest

prevalence of impaired fasting glucose and diabetes occurs in the 50-69 year group, often associated with obesity, hypertension, and dyslipidemia [72]. Whiting *et al*. (2011) similarly observed that diabetes prevalence increases with advancing age [73]. Kadiki and Reddy *et al*. (1996) also reported high rates of diabetes in obese young adults, though the burden remained higher in older groups [74]. Thomsen *et al*. (2018) identified that patients with early-onset T2DM (<45 years) exhibited obesity, dyslipidemia, and sedentary lifestyles, but the general trend remains that T2DM predominates in older populations [75]. Thus, while young-onset diabetes is increasing, particularly in obese individuals, the overall burden is expected to rise with longer life expectancy in older populations.

The clinical presentation of our participants also aligned with published data. In our study, 24% reported osmotic symptoms, 16% had weight loss, and none presented with ketosis, while the majority (60%) were diagnosed incidentally. The American Diabetes Association (2022) has stressed the importance of recognizing such features for timely diagnosis and management [76].

The present study demonstrated a significant age-related decline in both serum testosterone and 25-(OH)-Vitamin D levels among Kashmiri men with Type 2 Diabetes Mellitus (T2DM). The highest testosterone concentrations were observed in the 20-29 years age group, with a steady decline in subsequent decades, reaching the lowest levels in the 50-59 years group. Similarly, serum Vitamin D levels followed this downward trend, with younger men having higher concentrations and older men showing the lowest values. These findings are in accordance with previous studies which reported that T2DM is frequently associated with age-related hypogonadism and reduced Vitamin D synthesis. Cheung *et al*. (2015) demonstrated that a substantial proportion of men with T2DM present with low testosterone levels relative to age-specific reference ranges [77]. Similarly, Sollid (2016) emphasized that aging is accompanied by diminished Vitamin D production due to reduced sun exposure, impaired cutaneous synthesis, and altered metabolism [78]. Monapati *et al*. (2023) further highlighted the role of Vitamin D in glucose metabolism and insulin sensitivity, reinforcing its importance in diabetic men [79].

Another important finding was the inverse association of body mass index (BMI) with both testosterone and Vitamin D. Testosterone levels were highest in underweight men and lowest in obese participants, in agreement with previous studies showing that obesity contributes to hypogonadism through enhanced aromatization of testosterone to estrogen [80,81]. Similarly, Vitamin D levels decreased progressively with increasing BMI, a finding consistent with Jha *et al*. (2020), who reported that lower Vitamin D was linked to poorer glycemic control in T2DM [82]. Brijesh and Saurav (2014), as well as Usluogullari *et al*. (2015), also demonstrated a high prevalence of Vitamin D deficiency in T2DM patients [83]. Together, these findings highlight the synergistic effects of obesity and diabetes on hormonal dysregulation.

Duration of diabetes also played a critical role. Participants with a shorter diabetes duration (1-5 years) had significantly higher testosterone and Vitamin D levels compared to those with long-standing disease (>20 years). This is in agreement with Maresch *et al*. (2018) and Shaikh *et al*. (2016), who reported progressive testosterone decline with prolonged diabetes duration due to chronic hyperglycemia and testicular dysfunction [84,85]. Barkabi-Zanjani *et al*. (2020) similarly noted that prolonged hyperglycemia contributes to testicular impairment [86]. Wimalawansa (2016, 2018) and Hu *et al*. (2021, 2022) also confirmed that age, BMI, and duration of diabetes act as determinants of testosterone and Vitamin D status, reinforcing our findings [87,88].

Blood pressure parameters further underscored the clinical significance of hypogonadism in this cohort. Men with low testosterone (<300 ng/dl) exhibited significantly higher systolic and diastolic pressures. The Hypertension in Diabetes Study (1993) demonstrated the burden of hypertension in diabetics and its contribution to cardiovascular risk [89]. Yaron *et al*. (2009) reported that low testosterone is associated with arterial stiffness and impaired vascular relaxation [90]. Kelly *et al*. (2013) further highlighted that testosterone has vasodilatory effects on vascular beds and can improve cardiac ischemia [91,92]. Malipatil *et al*. (2019) concluded that low testosterone is associated with higher cardiovascular mortality in diabetic men [93]. Although HbA1c differences between low and normal testosterone groups were not statistically significant, the trend toward poorer glycemic control in the hypogonadal group supports earlier findings by Akarsu *et al*. (2017) and Kapoor *et al*. (2007) [22,94].

Hormonal evaluation revealed elevated LH and FSH in men with low testosterone, suggestive of hypothalamic-pituitary-gonadal (HPG) axis feedback. This observation is consistent with findings of Corradi *et al*. (2016), Sharma and Jayasena *et al*. (2022), and Mbiydzenyuy & Qulu (2024), who confirmed elevated gonadotropins as compensatory responses in primary hypogonadism [95-98]. Caroppo (2009) and Casteel & Singh (2020) also highlighted the complex interaction of the HPG axis in such cases [99,100].

With respect to metabolic risk, participants with low testosterone had lower HDL levels, consistent with Haring *et al*. (2011), who showed that hypogonadism is associated with dyslipidemia and cardiovascular risk [101]. Mårin *et al*. (1993) demonstrated improved insulin sensitivity with testosterone therapy [102]. More recent studies by Kapoor *et al*. (2006), Heufelder *et al*. (2009), Kalinchenko *et al*. (2010), and Jones *et al*. (2011) further confirmed that testosterone replacement improves glycemic control, lipid profile, and metabolic parameters in hypogonadal diabetic men [103-106].

An important aspect of our study was the strong positive association between Vitamin D and testosterone levels. Men with Vitamin D <20 ng/ml had lower testosterone compared to those with sufficient levels, supporting prior findings that Vitamin D receptors in Leydig cells modulate testosterone synthesis [107]. Jensen (2014) showed that Vitamin D signaling improves reproductive function [108,109], while Boisen *et al*. (2017) reported its role in calcium homeostasis and testicular function [110]. Moreover, Canguven *et al*. (2017) showed that Vitamin D supplementation modestly increases testosterone in deficient men [111]. Thus, the observed relationship in our study highlights a possible therapeutic role of Vitamin D in mitigating hypogonadism in T2DM.

Finally, the prevalence of hypogonadism in our cohort was strikingly high at 39.2%. Comparable studies have reported prevalence ranging from 18-25%. Al Hayek *et al*. (2014, 2017) demonstrated higher hypogonadism prevalence in diabetic men compared to non-diabetic counterparts, with associations to BMI, sexual dysfunction, and low socioeconomic status [112,114]. De Lorenzo *et al*. (2018) also reported hypogonadism in diabetics to be associated with reduced muscle mass, sexual dysfunction, and elevated cardiovascular risk [113].

Overall, this study underscores the strong interrelationship between testosterone, Vitamin D, BMI, duration of diabetes, and cardiovascular risk factors. The findings suggest that hypogonadism is a common but under-recognized complication in men with T2DM, particularly in those with obesity and long-standing disease. Early screening and intervention may help reduce associated metabolic and vascular complications in this high-risk population.

Conclusion

Prevalence of hypogonadism: Approximately 39.2% of men with T2DM had testosterone levels <300 ng/dl, highlighting a high prevalence of hypogonadism in this population.

Age-related hormonal decline: Both testosterone and Vitamin D levels decline with age, emphasizing the importance of early detection and management.

Impact of BMI: Obesity contributes to lower testosterone and Vitamin D levels, suggesting a need for weight management in diabetic men to prevent hormonal imbalances.

Diabetes duration: Longer diabetes duration correlates with lower testosterone and Vitamin D levels, indicating that prolonged diabetes exacerbates hormonal decline.

Hypertension and testosterone: Low testosterone is associated with higher blood pressure, pointing to potential cardiovascular risks in hypogonadal men with T2DM.

Hormonal regulation: Elevated LH and FSH levels in low testosterone groups suggest primary hypogonadism, possibly due to the testes' inability to respond adequately.

Vitamin D and testosterone link: Adequate vitamin D levels are crucial for maintaining testosterone levels, indicating a need for addressing vitamin D deficiency in this group.

Clinical implications: Early screening for low testosterone and vitamin D deficiency in diabetic men, especially those with higher BMI and longer diabetes duration, is critical for managing associated risks.

Future prospective: Further studies are needed to explore the therapeutic potential of vitamin D and testosterone regulation in improving metabolic health in men with T2DM.

Declarations

Ethics approval

The study was reviewed and approved by the ethical committee of our institute.

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Conflict of interest

None declared

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