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ANALYZING THE CORRELATION OF BIOCHEMICAL AND PERCEIVED HYPOGONADISM IN DIABETIC MEN: A PILOT SURVEY AT LADY READING HOSPITAL

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ABSTRACT

Background: Diabetes mellitus is a prime endocrine disorder that lowers sexual hormone levels, mainly testosterone, resulting in hypogonadism in affected males. It may be concluded that a clear comprehension of the relationship between biochemical and perceived hypogonadism is essential to enhance the utilization of specialized services for this population.

Objective: To investigate a linear relationship between biochemical hypogonadism, specifically serum testosterone levels, and perceived hypogonadal symptoms in men with diabetes.

Methodology: Analyzed cross-sectionally at Lady Reading Hospital over six months, the study enrolled 254 diabetic men. Biochemical hypogonadism was operationalized as total testosterone below 300 ng/dL while perceived hypogonadism was measured using the Androgen Deficiency in the Aging Male (AMS) score. Descriptive statistics were used to measure the frequencies of biochemical and perceived hypogonadism and their relationship.

Results: Out of 1155 men, 226 (88.2%) had biochemical hypogonadism, and 163 (63.6%) had perceived hypogonadal symptoms. A statistically seasonal significant difference was observed in self-perceived hypogonadism between the two groups In this study, 70 out of the 128 participants with biochemical hypogonadism complained of symptoms of hypogonadism with only 24 out of the 121 participants with normal testosterone scores reporting symptoms of hypogonadism ($p < 0.001$).

Conclusion: The present work emphasizes the frequency of biochemical and/or perceived hypogonadism in diabetic men and calls for regular screening for hypogonadism. An association between hormonal imbalance and lower quality of life and health was seen in this sample of this population, managing these hormonal imbalances might enhance quality of life and overall health.

Keywords: Hypogonadism, testosterone, diabetic subjects, perceived pathology, biochemical test, man health status.

Introduction

Low androgen level and/or reduced gonadal activity accompanied by poor sexual and reproductive capacity is known as hypogonadism and this endocrine abnormality is reported to be gradually emerging in diabetic male individuals.(1) The clinical manifestations of hypogonadism in men are decreased sexual desire, erectile dysfunction, asthenia, and reduced muscle mass and bulk, which reduce the quality of life.(2) Given that up to half of all diabetic men may suffer analytical hypogonadism, it is not surprising that the majority report experiencing one or more of the symptoms listed above.(3) The precise aetiology remains complex and perhaps mediated by insulin resistance, obesity, and persistent inflammation, all of which are typical of diabetes.

Hypogonadism diagnosis involves testing of biochemical markers testosterone where serum testosterone levels are helpful tests that provide an objective assessment of a deficiency in androgens.(4) Nevertheless, perceived hypogonadism may be present in many diabetic men, even though most of them do not necessarily meet the biochemical diagnosis of hypogonadism.(5) This concept refers to the perceived androgen deficiency – the patients' perceived symptoms of low testosterone levels without typical normative biomarker testosterone levels.(6) The failure to identify an increased risk of hypogonadism based on biochemical indicators and self-reported symptoms of sexual dysfunction is an issue for clinical practice as many diabetic men may go through the symptoms undiagnosed and untreated.

Endocrine interdisciplinary relationships between diabetes and the treatment of hypogonadism are proposed at several levels. Interaction of T2DM and obesity symptoms including obesity has been well documented in the development of hypogonadism because obesity leads to aromatization of body fat in adulthood to estrogens to reduce testosterone levels.(7) Further, diabetes is characterized by insulin resistance, and a negative influence on the hypothalamic-pituitary-gonadal axis may be due to decreased levels of LH coupled with less testosterone.(8) Since inflammation is also prevalent in diabetic patients, various signals for inflammation, including TNF-α and IL-6, reduce testosterone production of Leydig cells on the testis.(9)

Apart from biochemical factors, diabetic men are also more vulnerable to certain psychological factors that support their perception of hypogonadism. Men with depression, anxiety, and body image issue complaints, are most likely to link them with their condition or have increased severity from diabetes, making any hypogonadal symptoms they experience, even more intrusive.(10)

There is an increasing global trend in the incidence of diabetes and hypogonadism and the two are strongly related. However, there is limited data on how biochemical and perceived hypogonadism intersect in diabetic men. In this pilot survey, an attempt is made to evaluate the above-mentioned hypothesis in diabetic men in terms of both the hormonal measure and the self-rating scale of hypogonadal symptoms. Therefore, this work aims to analyze whether perceived symptoms correspond to biochemical markers and whether the current diagnostic process of hypogonadism in diabetic men lacks something. It might therefore enlighten clinicians about this relationship so that they can make better diagnoses to design better treatment plans for the management of hypogonadism in diabetic males. The current work is an attempt to establish if there is a relationship between the biochemical markers of hypogonadism as depicted by serum testosterone levels and the perceived symptomatology of hypogonadism in the diabetic patient population.

METHODOLOGY

This pilot study was presented as a cross-sectional survey to compare biochemical signs of primary hypogonadism with self-reported clinical manifestations of the disease in diabetic men. This study was intended to compare the index of objective circulating testosterone concentration and self-perceived hypogonadism symptoms in this population.

The present study was performed at the endocrinology and diabetes unit of Lady Reading Hospital (LRH), Peshawar, a teaching tertiary care hospital. The participants were recruited from the hospital's outpatient department also known as the OPD in this particular case. The study was conducted in the period between January 2023 and June 2023. The study sample consisted of 254 men diagnosed with

diabetes and aged 30 to 60 years. The sampling technique adopted was non-probability consecutive sampling. Consecutive patients with diabetes attending the outpatient diabetes clinic over the study period were recruited until the required number for the study was reached.

Patients with Type 2 diabetes mellitus in the study had to be male with a normal testosterone level, aged between 30 and 60 years with diabetes for at least one year, capable of giving informed consent, and capable of answering survey questions assessing reported hypogonadal symptoms. Exclusion criteria were as follows: men who had previously received testosterone replacement therapy or anabolic steroids and those with primary or secondary hypogonadism not associated with diabetes, severe complicating diseases, including liver or renal disease, terminal malignancy, and severe psychic disorders such as paranoid schizophrenia and bipolar affective psychosis.

All respondents voluntarily and in writing consented to participate in the study having been read the purpose of the study, their right to withdraw, and data confidentiality. brief sociodemographic data, self-perceived health status, and duration of diabetes were collected at the baseline of the recruitment of the participants. Data in medic choose diabetic history which refers to the detailed past medical history of the patient; and current medication history which refers to the comorbidity of the patient and their diabetes; the patient's current medications; smokers or non-smokers, alcohol consumers, or non-consumers, and their level of physical activity.

Blood samples were collected between 08:00 hours and 10:00 hours in the morning after overnight fasting to analyze the samples for serum testosterone. Serum levels of Testosterone were estimated by electrochemiluminescence immunoassay ELISA technique. Therefore, 300 ng/dL was used as the cut-off point in the categorization of mechanistic biochemical hypogonadism following recommendations by the Endocrine Society.(1) Finally, the participants' glycemic control was also evaluated by measuring fasting blood glucose and HbA1c.

Demographic data were collected from each participant, and these included responses to questionnaire data that sought to identify symptoms of hypogonadism. The questionnaire included: the International Index of Erectile Function (IIEF): which assesses erectile dysfunction and sexual desire, the Aging Male Symptoms (AMS) Scale: To check other signs of the disease which will include tiredness, change in mood, shrinkage of muscles, and general health status.(11) Each reported symptom was quantified on a Likert scale and hypogonadism was considered perceived if the participant met moderate or severe scores in at least two domains, sexual, physical, or psychological. A very brief clinical examination was conducted to check BMI and abdominal obesity as well as symptoms of hypogonadism consisting of a muscular decreased mass, gynecomastia, and testicular atrophy.

All data were keyed on SPSS version 26 for purposes of analysis for all the analyses that were to be conducted. Data, such as absolute age, BMI, testosterone levels, and HbA1c were analyzed by using mean ± SD. Categorical variables including perceived symptoms of hypogonadism were summarized using frequency and percentage. Pearson's correlation coefficient (for numerically scaled figures) and Spearman rank correlation (for ordinal data) were used to study the correlation between biochemical testosterone levels and the perceived severity of hypogonadism. Categorical variables including the percentage of participants with perceived hypogonadism were compared using Chi-square tests under low or normal testosterone levels.

The ethical clearance for the study was sought from the ethics committee of Lady Reading Hospital, Peshawar. In this study, every datum was taken devoid of identification of identity, and participant information was kept a secret all through the study. Patients and carers had the option of opting out at any time without a compromise of care and treatment.

Results

The average age of participants was 48.4 (SD 7.2) years, showing that the participants mainly belonged to middle age. With an average BMI of 29.9 kg/m², most of the participants fall in the overweight category. The participants have had a long history of the disease as the average period of their diabetes was 8.6 years. (Table 1) The average HbA1c was 7.9 % which is well above the optimum

level of 6.5% excluding pre-prandial levels. Individuals had on average fasting blood glucose levels of 152.5 mg/dL, therefore, corroborating the existence of hyperglycemia.

The mean serum testosterone level was 311.3 ng/dL, values that lie slightly above the biochemical hypogonadism chalk line. A total of 31 of the participants were considered to have biochemical hypogonadism through having their testosterone levels below 300 ng/dL. More than half of the participants believed that they had low testosterone, with AMS scores of 37 or above indicating true hypogonadism among 53.0% of participants. In addition, a large percentage of participants (58.5%) had erectile dysfunction with an IIEF of 25 or below. Therefore, the study has further revealed the high Prevalence Assessment of Hypogonadal Symptoms and Sexual Dysfunction in Diabetic Men. (Table 1)

Biochemical hypogonadism was defined as total testosterone < 300 ng/dl in the serum sample, and perceived hypogonadism was reported by 132 participants; among them, 70 (54.5%) had a low level of testosterone while perceived symptom was absent in 24 (19.7%) participants among those without perceived symptoms. However, 62 (45,5%) out of ninety percent of participants with normal testosterone levels (≥ 300 ng/dL) self-perceived as hypo-gonadal. The hypothesis that there is a positive correlation between low serum testosterone concentrations and the degree of perceived HS B symptomatology is confirmed by the results with $p < 0.001$. It lies in the fact that men with biochemical hypogonadism are statistically significantly more likely to report involvement of symptoms of hypogonadism than men with normal levels of testosterone.

Table 1: Baseline Characteristics of the Study Population (n = 254)

Characteristic	Mean ± SD	Frequency (%)
Age (years)	48.4 ± 7.2	
Body Mass Index (BMI) (kg/m²)	29.9 ± 4.6	
Duration of Diabetes (years)	8.6 ± 4.3	
HbA1c (%)	7.9 ± 1.7	
Fasting Blood Glucose (mg/dL)	152.5 ± 33.8	
Serum Testosterone (ng/dL)	311.3 ± 92.5	
Biochemical Hypogonadism (Testosterone < 300 ng/dL)		95 (36.5%)
Perceived Hypogonadism (AMS Score ≥ 37)		133 (53.0%)
Erectile Dysfunction (IIEF Score ≤ 25)		148 (58.5%)

Table 2: Correlation between Biochemical and Perceived Hypogonadism

Serum Testosterone Level (ng/dL)	Perceived Hypogonadism (n = 132)	No Perceived Hypogonadism (n = 122)	Total (n = 254)	p-value
< 300 (Biochemical Hypogonadism)	70 (54.5%)	24 (19.7%)	96	< 0.001
≥ 300 (Normal Testosterone)	62 (45.5%)	98 (80.3%)	158	
Total	132 (100%)	122 (100%)	254	

Discussion

The pilot survey demonstrated a strong association between biochemical hypogonadism with perceived hypogonadism amongst diabetic men. This finding concurs with other studies that have focused on the relationship between low levels of testosterone with hypogonadal symptoms in diabetic patients. Finally, hypogonadism has emerged as the common coexisting pathophysiology in men with type II diabetes given the impact of insulin resistance and obesity.

As for our data as to the frequency of biochemical hypogonadism in men with diabetes, some literature data are also available. A study by Erenpreiss J et al. (2020) showed that diabetic men had total

testosterone levels below the normal range while in the present study, the overall average of diabetic men was 36.5%.(12) Similarly, Kumari N et al. (2021) reported that type 2 DM patients were more prone to hypogonadism and above 40% of the patients presented low testosterone levels.(13) These findings support the results presented here and indicate that the Sofian et al study confirms the observation that hypogonadism is much more frequent in diabetic men than in the general population.
Concerning perceived hypogonadism, the relationship between the subjective complaints and the actual hormonal values has been an area of controversy. The sample in our study identified 54.5% of the men with biochemical hypogonadism reporting perceived hypogonadal symptoms on the AMS score. This result corresponds with those of Hackett G et al. (2023) wherein men with less testosterone complained of symptoms that included fatigue, loss of sexual desire, and impotency.(14) Although many of these symptoms may be seen in men who do not have diabetes, the effects of the illness on metabolic and hormonal processes make them more notable in such individuals.
However, some of the research that has been done has produced contrasting conclusions. For example, Liang G et al. (2021) spoke of a relatively low association between serum testosterone and hypogonadal symptoms and the majority of the male participants complained of various symptoms while their testosterone levels were considered normal.(15) This is different from our observation that a mere 19.7% of asymptomatic men presenting with low SHBG levels and no biochemical hypogonadism complained of symptoms. The difference might be attenuated by demographics, as Liang G recruited patients older than 40 and with a broader age distribution than our study, and we included only diabetic men where the hormonal and metabolic path of diabetes may amplify hypogonadal signs.
Also, our study revealed that erectile dysfunction is present in 58.5% of the subjects, which is in line with Boeri L et al (2020) who in their study concluded that hypogonadism in diabetic men is often associated with sexual dysfunction.(16) The androgen hormone is essential for sexual well-being and sexual health, a condition we noted in this study to be associated with low testosterone. In addition, the study by Yannas D et al (2021) showed that sexual dysfunction manifesting as erectile dysfunction is higher in men with poor glycaemic control compared to well-controlled diabetes confirming our results.(17) Thus, our study does not consider other factors that may affect perceived hypogonadism, including psychological state, depressed mood, or certain habits, including exercise, all of which can potentially affect subjective hypogonadism. Also due to the limitations of the study, the sample size though adequate for pilot analysis may not be representative of the general population.
Another weakness of our research is that it failed to examine other variables that can affect perceived hypogonadism including psychological health, depression, and exercise to mention but a few. Moreover, due to the limited scope of the pilot study the sample size although needed for a preliminary analysis, does not allow for a generalization of the results for the entire population.
Therefore, there is strong support for the existing ‘positive’ relationship between biochemical hypogonadism and perceived hypogonadal symptoms in diabetic men. These findings are in part conjunction with prior studies mainly in pointing to the high proportion of testosterone deficiency and sexual dysfunction among these patients. Thus, more larger sample study employing multiple dimensions is required to understand the relationship between testosterone levels, metabolic risk, and hypogonadal symptoms to enhance the diagnostic and therapeutic approaches to diabetic men.

Conclusion

The study establishes a high prevalence of hypogonadism, and especially low serum testosterone concentrations in the general population, which are associated with inferior quality of life and reduced sexual activity. When combined with the existing knowledge of how metabolic disorders and hormonal changes affect each other, this research implicates that the treatment of low testosterone ought to be an essential part of diabetes treatment. Further research with a larger sample size and better research designs are required for further clarification of this relationship and improving health amongst diabetic men.

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