How to Cite:
Jheetay, S., Garg, R., Adhana, R., Kumar, J., & Muniyal, H. (2022). The associations between serum dihydrotestosterone levels, lipid parameters & anthropometric measurements in male patients with type 2 diabetes mellitus. *International Journal of Health Sciences*, *6*(S4), 8585–8599. https://doi.org/10.53730/ijhs.v6nS4.10706

The associations between serum dihydrotestosterone levels, lipid parameters & anthropometric measurements in male patients with type 2 diabetes mellitus

Sanket Jheetay
PhD Scholar, Department of Physiology, Santosh Deemed to be University, Ghaziabad, U.P.
Corresponding author email: sanketjh@gmail.com

Rinku Garg
Professor & H.O.D, Department of Physiology, Santosh Deemed to be University Ghaziabad, U.P.

Ritu Adhana
Professor, Department of Physiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, U.P.

Jayballabh Kumar
Professor & H.O.D, Department of Physiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, U.P.

Himani Muniyal
Demonstrator, Department of Biochemistry, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, U.P.

***Abstract*---**Background: Male fertility is affected by the metabolic and hormonal dysregulation brought on by Diabetes Mellitus, a metabolic illness, particularly in the hypothalamus-pituitary testicular axis. However, there is little proof that endocrinopathy causes diabetic men's infertility and low testosterone levels. It is well established that Type 2 Diabetes causes dyslipidemia & obesity by lowering serum testosterone levels. However, there isn't much research on DHT, the most potent androgen, and its relationship to male lipid profiles. Methods: The study was carried out at Teerthanker Mahaveer Medical College and Research Centre, Moradabad, in the Department of Physiology and Medicine & Department of Physiology Santosh Medical College, Ghaziabad. A total of 210 samples—105 from type 2 diabetics and 105 from controls—were included in the study. Using

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
Manuscript submitted: 27 April 2022, Manuscript revised: 18 June 2022, Accepted for publication: 9 July 2022

conventional biochemical techniques, Lipid parameters [HDL, LDL, VLDL &TC], serum DHT, Data analysis was done with SPSS 26. [trial version]. Results: The levels of serum dihydrotestosterone were significantly lower in diabetic cases than in healthy controls [439.26 ± 257.87pg/ml vs 230.66 ± 182.02pg/ml, p=0.001]. 90 percent of Type 2 diabetics were found to have subnormal levels, as opposed to just 10 percent of controls. In the research, 15 out of the 105 participants had a BMI > 30 and were obese associated with diabetes. The typical BMI for people with diabetes was 26.99 ±3.01. In diabetic patients, the mean waist-to-hip ratio was 0.95.06 as opposed to 0.93.±05 in the control group [p=0.010]. The weight in diabetes patients is 79.55 kg; in the control group, it is 71.03 kg; [p 0.001]. Low DHT levels were associated with lower HDL levels in people with diabetes [37.50–±14.76 mg/dL], whereas patients with normal DHT levels had significantly higher mean HDL values [49.02–±7.93 mg/dL]. Low DHT levels were also associated with comparable VLDL, TG, and TC patterns. Conclusion: Males with Type 2 diabetes had significantly reduced DHT levels, and DHT worsened as the lipid profile worsened.

***Keywords*---**dihydrotestosterone, type 2 diabetes mellitus, lipid profile, wasit hip ratio, BMI.

Introduction

Over 0.4 billion people worldwide have diabetes, and its incidence is still rising noticeably every year. Diabetes is a public health concern. [1] These disorders include type 2 diabetes mellitus [T2DM], a group of related conditions in which the body cannot control the quantity of glucose in the blood. This is a consequence of insulin resistance [IR], which is defined as the target organs' inability to react appropriately to the action of insulin. Insulin needs to rise due to insufficient reduction of hepatic glucose production and decreased insulin-mediated glucose absorption in the peripheral [skeletal muscle and adipose tissue] [Adilson et al., 2008]. The results of IR include impaired insulin action, which is referred to as the initial stage of type 2 diabetes [T2DM], as well as glucose intolerance, hyperglycemia, hyperinsulinemia, dyslipidemia, hormonal imbalance, cardiovascular disease, peripheral neuropathy, stroke, infection, chronic renal failure, retinopathy, and other conditions. [1,2,3] Among endocrine disorders, diabetes mellitus is the most prevalent. The hypothalamus and anterior pituitary, two of the three parts of the male reproductive system, only have regulatory activities that are mediated by their hormones. A traditional negative feedback mechanism manages this well-tuned hypothalamic-pituitary-gonadal axis. [4, 5] Due to metabolic and hormonal dysregulation, notably in the hypothalamus-pituitary testicular axis, Diabetes Mellitus, a metabolic disorder, impairs male fertility. But there is scant evidence that endocrinopathy is the main factor in diabetic men's infertility & low androgens in men. [6] Testes and the adrenal cortex create the steroid hormone testosterone. The precursor molecule for DHT production is cholesterol, and following a series of processes, it is converted into testosterone.[7] With the aid of the enzyme 5-alpha-reductase, testosterone is converted to the other active hormones 5- dihydrotestosterone

[DHT]. DHT causes numerous virilising effects of testosterone. DHT is a lot stronger than the other androgens. [8] Male sexual development is greatly influenced by DHT, which first appears early in foetal life. The development of the male external genitalia depends on it. The genital tubercle, urogenital fold, labio-scrotal folds, and circulating foetal testosterone are properly differentiated in males thanks to the peripheral 5-alpha-reductase type 2 enzyme. This process results in the development of the prostate, scrotum, and penis development. DHT aids in promoting the gubernacular development necessary for testicular descent and insulin-like factor 3 (INSL30).[8,9] The DHT encourages the penis and scrotum to develop and mature. The main androgen responsible for the development of pubic, body, face, and body hair is DHT. Only 10% as much DHT as testosterone is circulating in the blood at any time. However, because DHT is only produced in peripheral tissues, its level can be up to 10 times higher than testosterone.[9,10] The suppression of testosterone [T] production is a direct effect of DM on testicular secretory function (Corona et al., 2011; Ding et al., 2006; Pitteloud et al., 2005). Evidence suggests that T deficit is found in 40% of males with type 2 diabetes mellitus (T2DM). These figures might be made worse since pre-diabetes (PreD), the prodromal stage of diabetes, also affects T levels (Rato et al., 2013). This is critical because a loss in male reproductive health is being caused by the large drop of testosterone caused by diabetes conditions (Corona et al., 2011; Dhindsa et al., 2004; Pitteloud et al., 2005; Rato et al., 2013; Rato et al., 2014b). Low T levels are believed to be intimately linked to the many problems that affect the reproductive tract as well as in testicular cells, notably in Sertoli cells (Bernardino et al., 2013). (Pitteloud et al., 2005; Rato et al., 2013; Zitzmann, 2009).[11,12] The physiology of Sertoli Cells is impacted by testosterone and its metabolites, such as 5-DHT (Fukami et al., 2013; Robaire and Viger, 1995).[13] The idea behind spermatogenesis is that male fertility relies on the Sertoli cell's metabolism, which is strictly controlled by the hormone 5-DHT (Oliveira et al., 2011; Rato et al., 2012). However, it is unclear if the lowered T levels brought on by subsequent stages of DM might impact the metabolic behaviour of Sertoli cells. [10,14] A key factor in preserving glucose homeostasis is insulin's ability to increase glucose absorption in peripheral tissues including muscle and fat, reduce hepatic glucose production, and regulate lipid metabolism. By promoting GLUT4's translocation to the plasma membrane, insulin aids in transporting glucose from the blood. Any additional glucose is converted to the production of fatty acids once the liver is fully stocked with glycogen. (15,16). Insulin is connected to additional triglyceride production in fat cells, which causes an increase in fat storage in adipose tissue. [17] Despite hyperinsulinemia, there is a decrease in the tissue's ability to react to insulin in situations of insulin resistance. (18) Due to the excess of fatty acids in plasma, the liver is encouraged to convert part of the fatty acids into phospholipids and cholesterol, two of the main byproducts of fat metabolism. As a result, the body behaves like it is fasting in an insulin-absence condition (Blaschke et al., 2006). [19] These two compounds are released into the blood as lipoproteins with their co-receptors, such as Apo Al and Apo B, Apo E, resulting in a rise in serum cholesterol, triglycerides, and LDL. These substances also cause the liver to produce extra triglycerides at the same time. [20,21] Greater levels of endogenous DHT are typically associated with a better cardiovascular profile, including lower triglyceride levels, higher HDL cholesterol, lower blood sugar and blood pressure, according to the cross-sectional research. Further study is needed to determine if low DHT only acts as a coexisting biomarker for

diabetes or whether it has a role in the pathophysiology of the disease. There is a major paucity of this kind of study in India. As a result, the current study's objective is to evaluate the blood dihydrotestosterone levels of type 2 diabetic males and search for any significant lipid profile associations.

Material and Methods

Selection of study group

The 105 male patients in this study who were diagnosed with Type 2 DM [according to WHO criteria FBS > 126 mg/dl and HbA1c > 6.5%] and the 105 healthy men who were selected as controls were all above the age range of 30 to 60, once the ethics commission has given its permission.

Study setup

This study was conducted in the Department of Physiology and Department of Medicine of Teerthanker Mahaveer Medical College and Research Centre, Moradabad and the Department of Medicine of Santosh Medical College, Ghaziabad.

Study design

This is an observational and comparative case-control study.

Inclusion and exclusion criteria

Male patients with Type 2 Diabetes Mellitus between the ages of 30 and 60 were included as research participants. Patients with ages between 30 and 60, those who were prescribed finasteride, epristeride, alfa-radiol, and saw palmetto extract, those who were receiving treatment for benign prostatic hyperplasia and prostate cancer, patients with liver diseases, those with a history of chronic alcoholism, and those who had smoked continuously for more than 10 years were all excluded from the study.[22]

Sample size

The sample size was 105 diabetic cases and 105 controls based on the calculated prevalence of DM type 2 in Western Uttar Pradesh(Moradabad).

Methods for estimation

1. Serum glucose estimation by GOD POD Method. [23]
2. Estimation of HbA1c using Boronate Affinity Chromatography. [24]

3. Determination of total cholesterol by CHOD PAP Method. [25]
4. Determination of serum triglycerides by Glycerol oxidase- Trinder method, endpoint method. [26]
5. Determination of HDL-Cholesterol by Modified polyethene glycol precipitation method. [27]
6. Serum LDL-Cholesterol was calculated by Friedwald's formula. [28]
7. Estimation of Serum Dihydrotestosterone levels by using Enzyme-Linked Immunosorbent Assay(ELISA). [29]

Data management and analysis plan

The statistical analyses were performed using SPSS version 26. The descriptive results were expressed as mean ± standard.

Results

Table 1 : Age distribution of study participants

	DIABETIC CASES	CONTROL	Total
GROUP	N	N	N
31-40	17	22	39
41 – 50	29	40	69
51 – 60	59	43	102
Tota	5	105	210
MEAN	49.84±7.88	47.79±7.55	48.81±7.74

Table 1 displays the research subjects' age distribution. The age range of 51 to 60 years represented the greatest number of diabetes patients in this research.

Table 2: Distribution of study population according to bmi

BMI Range	DIABETIC CASES[n=105]	CONTROLS [n=105]	Total
	N	N	N
18-24.99	33	84	117
25-29.99	57	16	73
30 and above	15	5	20
Total	105	105	210

Mean	26.99±3.01	23.78± 2.41	25.39±3.17

An analysis of body mass index in diabetes patients revealed that on average (n=57), patients had a BMI between 25 and 29.99, which indicates that they were overweight. 15 out of the 105 individuals had a BMI over 30, making them obese. For those with diabetes, the average BMI was 26.99± 3.01. In contrast, the majority of individuals (n=84) in the control group had BMIs between 18 and 24.99; the control group's mean BMI was 23.78± 2.41.

Table 5: Comparison of anthropometric parameters between diabetic cases and controls

Parameters	Diabetic Cases		Control group		t-value	p-value
	Mean	Standard deviation	mean	Standard deviation		
Waist_Hip Ratio	0.95	0.06	0.93	0.05	2.60	0.010
WEIGHT[Kgs]	79.55	9.06	71.03	7.19	7.51	<0.001

The waist to hip ratio and weight of the diabetic patients and the control group differ significantly, as seen in the above table. The mean waist-to-hip ratio for diabetic cases was.95.06, compared to 0.93±05 for the control group (p=0.010). In diabetic cases, the weight is 79.55 ± 9.06 kg, but in the control group, it is 71.03± 7.19 kg (p 0.001).

Table 4 : Comparison of blood pressure between diabetic cases and controls

Parameters	Diabetic Cases		Control group		t-value	p-value
	Mean	Standard deviation	mean	Standard deviation		
Systolic Blood Pressure[mm of Hg]	137.30	11.58	133.46	9.85	2.5	0.01
Diastolic Blood Pressure [mm of Hg]	85.19	6.14	82.39	6.77	3.1	0.002

Table 4 demonstrates that there was a substantial rise in both systolic and diastolic blood pressure in diabetes patients when their blood pressure was compared to that of controls.

Table 5: comparison of levels of fasting blood glucose, post prandial and HBA1C between diabetic cases and controls

Parameters		Diabetic Cases		Control group		t-value	p-value
		Mean	Standard deviation	Mean	Standard deviation		
1.	Fasting blood sugar [mg/dL]	161.96	24.16	85.01	8.56	30.767	0.000
2.	PP[mg/dL]	163.40	24.21	109.68	15.42	19.187	0.000
3.	HbA1c[%]	7.18	1.30	4.44	0.77	18.633	0.000

Table 5 compares the predicted FBG, PP, and HbA1c values between healthy controls and Type 2 Diabetes Mellitus patients. The table clearly shows that individuals with type 2 DM had significantly higher levels of FBG, PP, and HbA1c when compared to controls (p 0.001). In diabetic patients, the mean fasting plasma glucose levels were 161.96 ± 24.16 mg/dl, compared to 85.01 ± 8.56 mg/dl in controls. The mean post-meal values in diabetes individuals were 163.40 ± 24.21 mg/dl, compared to 109.68 ± 15.42 mg/dl in control cases. HbA1c values for diabetes patients were 7.18 ± 1.30 percent on average, compared to 4.44 ± 0.77 percent for controls.

Table 6: Comparison of lipid parameters between diabetic cases and controls.

Parameters		Diabetic Cases		Control group		t-value	p-value
		Mean	Standard deviation	Mean	Standard deviation		
1.	HDL[mg/dL]	45.94	11.35	52.83	9.38	4.79	<0.001
2.	LDL[mg/dL]	139.24	45.46	105.25	37.19	5.93	<0.001
3.	VLDL[mg/dL]	38.27	11.33	29.41	15.64	4.69	<0.001
4.	TG[mg/dL]	191.34	56.66	147.05	78.21	4.69	<0.001
5.	TC[mg/dL]	223.45	49.46	187.49	40.93	5.74	<0.001

The mean value of the lipid parameters evaluated in the current study is displayed in Table 6. In diabetic cases, LDL, VLDL, triglycerides, and total cholesterol levels were considerably higher. For diabetic cases, the HDL was 45.94± 11.35 mg/dL, compared to 52.83± 9.38 mg/dL for the control group (p .001). For diabetic cases, LDL was 139.24± 45.46 mg/dL, compared to 105 ± 37.19 mg/dL for the control group. The VLDL levels in the diabetic patients and control group were 38.27± 11.33 mg/dL and 29.41± 15.64 mg/dL, respectively. Triglycerides for diabetic cases were 191.34± 56.66 mg/dL, compared to 147.05± 78.21 mg/dL for the control group. For diabetic patients and the control group, the total cholesterol levels were 223.45± 49.46 mg/dL and 187.49± 40.93 mg/dL, respectively.

Table 7: Comparison of serum levels of dihydrotestosterone between diabetic cases and controls

Parameters		Diabetic Cases		Control group		t-value	p-value
		Mean	Standard deviation	mean	Standard deviation		
1.	DHT[pg/ml]	230.66	182.02	439.26	257.87	-6.77	<0.001

In the control group, the DHT was 439.26± 257.87 pg/ml, which was considerably higher in the population without diabetes (p 0.001). The DHT in diabetic cases was 230.66 ±182.02 pg/ml.

Table 8 : Comparison between serum level of dihydrotestosterone with lipid parameters in subjects with type II diabetes mellitus.

Lipid profile	DHT levels				F-factor	p-value
	Below normal [<112pg/mL]		Normal[112-955 pg/mL]			
	Mean	SD	Mean	SD		
HDL	37.50	14.76	49.02	7.93	26.32	<0.001
LDL	156.94	46.80	132.81	43.50	6.06	0.015
VLDL	44.60	11.54	35.96	10.40	13.35	<0.001
TG	223.02	57.70	179.81	52.02	13.35	<0.001
TC	239.04	51.20	217.79	47.91	3.89	0.051

It was shown that diabetic individuals with low DHT levels had lower HDL levels (37.50±14.76 mg/dL), whereas patients with normal DHT levels had considerably

higher mean HDL values (49.02±7.93 mg/dL). In comparison to patients with normal DHT (132.81±43.50), patients with DHT below the normal category (156.94±46.80 mg/dL) had considerably higher LDL values. In patients with low DHT levels, the levels of VLDL, TG, and TC exhibited similar trends.

Discussion

Obesity and overweight are defined as an excessive accumulation of adipose tissue that negatively impacts one's physical and mental health and well-being. [30] Type 2 diabetes and obesity are both correlated with insulin resistance. The nonesterified fatty acids (NEFAs) that are produced from adipose tissue in obese people support the idea that insulin resistance and beta-cell dysfunction are most likely connected.[30,31] Persons with insulin resistance, whether thin or overweight, have higher insulin responses and less hepatic insulin clearance than individuals with insulin sensitivity. [30] The age distribution of the study participants is shown in Table 1. Most diabetes cases (59 out of 105) were found in people between the ages of 51 and 60. The maximum number (43 out of 105) is also seen in the same age range in the controls group. This demonstrates that this study is age-matched. In Table 2 we analysed body mass index which revealed that in diabetic cases 15 out of 105 patients were obese, defined as having a BMI of more than 30 and that the majority of patients (n=57) had BMIs between 25 and 29.99. The BMI for men with diabetes was 26.99± 3.01. In contrast, the majority of individuals (n=84) in the control group had BMIs between 18 and 24.99. The control group's mean BMI was 23.78± 2.41. The risk of metabolic illnesses such as type 2 diabetes mellitus, hypertension, and dyslipidemia is often correlated with an increase in body fat. [32] Moreover, the majority of individuals with these metabolic illnesses are fat or overweight. It is therefore a two-way connection. One of the probable causes of insulin resistance, which raises blood sugar or glucose levels and eventually results in diabetes, is overeating. [33] Gupta et al. found during their analysis that a higher BMI raises the risk of both diabetes and prediabetes. Additionally, those who are overweight or obese have a higher chance of developing this condition than those who are not. These findings are in line with studies by Sepp et al. and Huffman et al., which show a positive relationship between rising BMI and blood glucose levels and diabetes. [34.35] The waist-hip ratio and weight of the diabetes patients and the control group were significantly different, as shown in Table 5. In diabetic patients, the mean waist-to-hip ratio was 0.95 ±06, compared to 0.93 ±05 in the control group [p=0.010]. The weight in diabetes patients is 79.55 ±9.06 kg against 71.03 ±7.19 kg in the control group [p 0.001]. Abtahi et al. also observed that the prevalence of preDM was higher in an obese person having a higher range of waist circumference, WHR and BMI. Body weight is determined by many factors such as genetic, behavioural, cultural, socio-economic, physical inactivity, diet and psychosocial factors. [36] In their study, Koshki et al. found a substantial direct correlation between WC and WHR and the likelihood of developing diabetes. For every 10 cm rise in WC and 10 percent increase in WHR, the risk rose by 23%. [37] When the blood pressure of diabetes patients was compared to that of controls, Table 4 demonstrated that there was a substantial rise in both systolic and diastolic blood pressure in diabetic patients. The Mean value of systolic blood pressure in diabetic males was 137.30 + 11.58mm of Hg whereas in controls was 133.46 + 9.85 mm of Hg. Whereas the mean value of diastolic Blood pressure in diabetic cases was 85.19 +

6.14 mm of Hg and in controls was 82.39 + 6.77 mm of Hg. Diabetes and hypertension usually co-exist. Diabetes and hypertension have many similarities in their etiologies and pathophysiology. Obesity, inflammation, oxidative stress, and insulin resistance are thought to be shared processes. [38] The estimated FBG, PP, and HbA1c values for Type 2 Diabetes Mellitus patients and healthy controls are contrasted in Table 5. The data demonstrate unequivocally that as compared to controls, those with type 2 DM had considerably higher levels of FBG, PP, and HbA1c [p 0.001]. The mean fasting plasma glucose levels in diabetes patients were 161.96± 24.16 mg/dl as opposed to 85.01± 8.56 mg/dl in controls. In those with diabetes, the mean post-meal readings were 163.40± 24.21 mg/dl as opposed to 109.68± 15.42 mg/dl in control cases. Diabetes patients' average HbA1c readings were 7.18± 1.30 percent, compared to controls' 4.44± 0.77 percent. Table 6 shows the mean value of the lipid parameters assessed in the current investigation. LDL, VLDL, triglyceride, and total cholesterol levels were significantly higher in diabetes patients. In diabetes patients, HDL was 45.94± 11.35 mg/dL, whereas the control group's HDL was 52.83± 9.38 mg/dL. [p .001]. LDL was 139.24± 45.46 mg/dL in diabetes individuals against 105± 37.19 mg/dL in the control group. The VLDL values in the control group and diabetes patients were 29.41 mg/dL and 38.27 mg/dL, respectively. Triglycerides were 191.34±56.66 mg/dL in diabetic individuals against 147.05±78.21 mg/dL in the control group. Total cholesterol levels were 223.45±49.46 mg/dL for diabetic patients and 187.49±40.93 mg/dL for the control group, respectively. It was shown that patients with normal DHT levels had significantly higher mean HDL values (49.02±7.93 mg/dL), whereas diabetics with low DHT levels had lower HDL levels (37.50±14.76 mg/dL). In comparison to patients with normal DHT (132.81±43.50), patients with DHT below the normal category (156.94±46.80 mg/dL) had considerably higher LDL values. The levels of VLDL, TG, and TC demonstrated comparable patterns in patients with low DHT levels. People with T2DM and impaired glucose tolerance have greater triglyceride levels and more HDL is catabolized, which lowers HDL levels. [39] Numerous potential pathways might account for the negative correlation between increased HDL catabolism in insulin resistance states and hypertriglyceridemia, which leads to decreased plasma HDL concentrations. Reduced lipoprotein lipase (LPL) activity is one of the causes, and this might have an impact on how efficiently HDL particles develop. The usual insulin-mediated stimulation of LPL activity has been shown to be diminished in individuals with insulin resistance. When glycemic management is poor in individuals who are somewhat insulin-deficient, LPL activity is lowered in T2DM. [39,40,41,42] Our results are consistent with Rongtao Cui, Zhiming Qi, and Junyong Zhang's observations that type 2 T2DM is more common in Chinese adults with low HDL-C, high TG, and excessive levels of BMI and waistline. [d13] Comparing DHT levels between patients with Type 2 DM and controls is shown in Table 7. DHT levels were found to be considerably higher in people without diabetes. While the DHT in the control group was 439.26± 257.87 pg/ml, it was much higher in the population without diabetes. The DHT in the study group was 230.66± 182.02 pg/ml. There is reasonably consistent evidence that Testosterone has a relationship with androgen in men only a few studies have examined DHT, which is produced from the conversion of T by 5-*a*-reductase and a more potent androgen than T. This partly reflects the difficulty in measuring DHT levels, which are approximately 10-fold lower than circulating T levels.[43] Numerous mechanisms have been proposed to account for the links between androgens and

both insulin resistance and diabetes. For instance, DHT and T have been linked to fat accumulation in male cohorts of both young and elderly, according to Vandenput et al. Experimental studies employing male mice missing the androgen receptor have shown that androgens have a role in the accumulation of late-life obesity. Collectively, these results suggest that androgens reduce fat accumulation; as a result, greater levels of androgens protect against insulin resistance and lessen the risk of developing diabetes. [10,44,45] Our results concur with those of Mather et al., who discovered an inverse relationship between T and DHT and fasting glucose levels in middle-aged males. [46] Table 8 demonstrates that although diabetic men with normal DHT levels had higher mean HDL levels (49.02±7.93 mg/dL), diabetic men with low DHT levels had lower HDL levels (37.50±14.76 mg/dL). In comparison to patients with normal DHT (132±43.50 mg/dL), patients with DHT below normal category (156.94±46.80 mg/dL) had considerably higher LDL values. In patients with low DHT levels, the levels of VLDL, TG, and TC exhibited similar patterns. In their investigation of males with cardiovascular disease, Page et al. found that DHT and HDL-C had a positive correlation (P = 0.0128 for the correlation between DHT and HDL-C). This was comparable to the current research. [46,47] The present study shows that factors such as BMI, waist circumference and lipid profile were associated with low DHT levels in male patients with type 2 diabetes mellitus. Low DHT levels are also related to hyperlipidaemia, increased waist-hip ratio and visceral fat accumulation. It seems that low androgen levels increase artery stiffness in men with type 2 diabetes mellitus. To know the exact mechanism of how DHT affects the lipid profile more studies with greater sample sizes are required in future. Therefore, we conclude that there is a possibility that early measurement of levels of DHT with might help to decrease the chances of complications associated with type 2 diabetes mellitus and progression of the disease itself to improve which can lead to a better quality of life.

Conclusion

This study showed that DHT levels were significantly low in males with type 2 diabetes mellitus as compared to controls with $p< 0.001$. There was a significant increase in levels of total cholesterol, LDL and triglycerides in patients with type 2 diabetes mellitus whereas HDL levels were low. Most of the patients with type 2 diabetes mellitus were overweight with an increased waist-hip ratio. We also observed that diabetic males with low serum DHT levels had fewer HDL levels also while the patients with normal DHT had more HDL levels. The levels of VLDL, TG, TC and LDL were significantly more in patients with low levels of DHT. Therefore, the study concludes that androgen DHT affects the lipid profile thereby increasing the risk of cardiovascular disease.

References

1. Adveetabiotech.com. [cited 2022 Jun 30]. Available from: https://adveetabiotech.com/wp-content/uploads/2020/05/21_Triglycerides-_Test_Kit.pdf
2. Algoblan A, Alalfi M, Khan M. Mechanism linking diabetes mellitus and obesity. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2014;:587.

3. Alves MG, Martins AD, Vaz CV, Correia S, Moreira PI, Oliveira PF, et al. Metformin and male reproduction: Effects on Sertoli Cell metabolism. British Journal of Pharmacology. 2014;171(4):1033–42.
4. AMBADE VIVEKN, SHARMA YV, SOMANI BL. Methods for estimation of blood glucose : A comparative evaluation. Medical Journal Armed Forces India. 1998;54(2):131–3.
5. Bala M, Meenakshi, Aggarwal S. Correlation of body mass index and waist/hip ratio with glycated hemoglobin in prediabetes. EJIFCC. 2019;30(3):317–24.
6. Bays HE, Chapman RH, Grandy S. The relationship of body mass index to diabetes mellitus, hypertension and dyslipidaemia: Comparison of data from two national surveys. International Journal of Clinical Practice. 2007;61(5):737–47.
7. Biosciences E. Dihydrotestosterone (DHT) ELISA Assay Kit [Internet]. Eaglebio.com. [cited 2022 Jun 30]. Available from: https://eaglebio.com/wp-content/uploads/data-pdf/dht31-dht-elisa-assay-kit-packageinsert.pdf
8. Biotec-co.com. [cited 2022 Jun 30]. Available from: https://www.biotec-co.com/images/products/clinical_chemistry/kits/chemistry/Cholesterol.pdf
9. Blaschke F, Caglayan E, Hsueh WA. Peroxisome proliferator-activated receptor gamma agonists: Their role as vasoprotective agents in diabetes. Endocrinology and Metabolism Clinics of North America. 2006;35(3):561–74.
10. Cheung BMY, Li C. Diabetes and hypertension: is there a common metabolic pathway? Curr Atheroscler Rep [Internet]. 2012;14(2):160–6. Available from: http://dx.doi.org/10.1007/s11883-012-0227-2
11. Clark RV, Hermann DJ, Cunningham GR, Wilson TH, Morrill BB, Hobbs S. Marked suppression of dihydrotestosterone in men with benign prostatic hyperplasia by dutasteride, a dual 5α-reductase inhibitor. The Journal of Clinical Endocrinology & Metabolism. 2004;89(5):2179–84.
12. Costanzo PR, Suárez SM, Scaglia HE, Zylbersztein C, Litwak LE, Knoblovits P. Evaluation of the hypothalamic-pituitary-gonadal axis in EUGONADAL men with type 2 diabetes mellitus. Andrology. 2013;2(1):117–24.
13. Cui R, Qi Z, Zhou L, Li Z, Li Q, Zhang J. Evaluation of serum lipid profile, body mass index, and waistline in Chinese patients with type 2 diabetes mellitus. Clin Interv Aging [Internet]. 2016;11:445–52. Available from: http://dx.doi.org/10.2147/CIA.S104803.
14. de Luca C, Olefsky JM. Inflammation and insulin resistance. FEBS Letters. 2007;582(1):97–105.
15. Fan W, Yanase T, Nomura M, Okabe T, Goto K, Sato T, et al. Androgen receptor null male mice develop late-onset obesity caused by decreased energy expenditure and lipolytic activity but show normal insulin sensitivity with high adiponectin secretion. Diabetes [Internet]. 2005;54(4):1000–8. Available from: http://dx.doi.org/10.2337/diabetes.54.4.1000.
16. Femlak M, Gluba-Brzózka A, Ciałkowska-Rysz A, Rysz J. The role and function of HDL in patients with diabetes mellitus and the related cardiovascular risk. Lipids Health Dis [Internet]. 2017;16(1):207. Available from: http://dx.doi.org/10.1186/s12944-017-0594-3.
17. Guilherme A, Virbasius JV, Puri V, Czech MP. Adipocyte dysfunctions linking obesity to insulin resistance and type 2 diabetes. Nature Reviews Molecular Cell Biology. 2008;9(5):367–77.

18. Guilherme A, Virbasius JV, Puri V, Czech MP. Adipocyte dysfunctions linking obesity to insulin resistance and type 2 diabetes. Nature Reviews Molecular Cell Biology. 2008;9(5):367–77.
19. Gupta S, Bansal S. Correction: Does a rise in BMI cause an increased risk of diabetes?: Evidence from India. PLOS ONE. 2021;16(2).
20. HDL Cholesterol precipitating reagent set [Internet]. Biopacific.net. [cited 2022 Jun 30]. Available from: http://www.biopacific.net/wp-content/uploads/2016/07/Pointe-HDL-Cholesterol-PEG-Insert.pdf
21. Hirano T. Pathophysiology of diabetic dyslipidemia. J Atheroscler Thromb [Internet]. 2018;25(9):771–82. Available from: http://dx.doi.org/10.5551/jat.rv17023.
22. Home - books - NCBI [Internet]. National Center for Biotechnology Information. U.S. National Library of Medicine; [cited 2022Jun29]. Available from: https://www.ncbi.nlm.nih.gov/books
23. Huffman MD, Fall CHD, Khalil A, Osmond C, Tandon N, Lakshmy R, et al. Association between anthropometry, cardiometabolic risk factors, & early life factors & adult measures of endothelial function: Results from the New Delhi Birth Cohort. Indian Journal of Medical Research. 2015;142(6): 1765–1774.
24. Introduction to lipids and lipoproteins - NCBI bookshelf [Internet]. [cited 2022Jun29]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK305896/
25. Jafari-Koshki T, Mansourian M, Hosseini SM, Amini M. Association of waist and hip circumference and waist-hip ratio with type 2 diabetes risk in first-degree relatives. J Diabetes Complications [Internet]. 2016;30(6):1050–5. Available from: http://dx.doi.org/10.1016/j.jdiacomp.2016.05.003.
26. Joyce KE, Biggs ML, Djoussé L, Ix JH, Kizer JR, Siscovick DS, et al. Testosterone, dihydrotestosterone, sex hormone binding globulin and incident diabetes among older men: The Cardiovascular Health Study. The Journal of Clinical Endocrinology & Metabolism. 2016;
27. Joyce KE, Biggs ML, Djoussé L, Ix JH, Kizer JR, Siscovick DS, et al. Testosterone, dihydrotestosterone, sex hormone binding globulin and incident diabetes among older men: The Cardiovascular Health Study. The Journal of Clinical Endocrinology & Metabolism. 2016;102(1):33-39
28. Kahn BB, Flier JS. Obesity and insulin resistance. Journal of Clinical Investigation. 2000;106(4):473–81.
29. Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature. 2006;444(7121):840–6.
30. Krishnaveni P, Gowda VM. Assessing the validity of Friedewald's Formula and anandraja's formula for serum LDL-cholesterol calculation. J Clin Diagn Res [Internet]. 2015;9(12):BC01-4. Available from: http://dx.doi.org/10.7860/JCDR/2015/16850.6870.
31. Maneesh M, Jayalakshmi H, Singh TA, Chakrabarti A. Impaired hypothalamic-pituitary-gonadal axis function in men with diabetes mellitus. Indian Journal of Clinical Biochemistry. 2006;21(1):165–8.
32. Marchetti PM, Barth JH. Clinical biochemistry of dihydrotestosterone. Annals of Clinical Biochemistry: International Journal of Laboratory Medicine. 2013;50(2):95–107.
33. Marks LS. 5alpha-reductase: history and clinical importance. Rev Urol. 2004;6 Suppl 9:S11-21.

34. Mather KJ, Kim C, Christophi CA, Aroda VR, Knowler WC, Edelstein SE, et al. Steroid sex hormones, sex hormone-binding globulin, and diabetes incidence in the Diabetes Prevention Program. J Clin Endocrinol Metab [Internet]. 2015;100(10):3778–86. Available from: http://dx.doi.org/10.1210/jc.2015-2328.
35. Navarro G, Xu W, Jacobson DA, Wicksteed B, Allard C, Zhang G, et al. Extranuclear actions of the androgen receptor enhance glucose-stimulated insulin secretion in the male. Cell Metabolism. 2016;23(5):837–51.
36. Page ST, Mohr BA, Link CL, O'Donnell AB, Bremner WJ, McKinlay JB. Higher testosterone levels are associated with increased high-density lipoprotein cholesterol in men with cardiovascular disease: results from the Massachusetts Male Aging Study. Asian J Androl [Internet]. 2008;10(2):193–200. Available from: http://dx.doi.org/10.1111/j.1745-7262.2008.00332.x
37. Parhofer KG. Interaction between glucose and lipid metabolism: More than diabetic dyslipidemia. Diabetes Metab J [Internet]. 2015;39(5):353–62. Available from: http://dx.doi.org/10.4093/dmj.2015.39.5.353.
38. Pathogenesis of type 2 diabetes mellitus - NCBI bookshelf [Internet]. [cited 2022Jun29]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK279115/
39. Physiology, endocrine hormones - statpearls - NCBI bookshelf [Internet]. [cited 2022Jun29]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538498/
40. Physiology, Glucose Transporter Type 4 - NCBI Bookshelf [Internet]. [cited 2022Jun29]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537322/
41. Plant TM. 60 years of neuroendocrinology: The Hypothalamo-pituitary–gonadal axis. Journal of Endocrinology. 2015;226(2).
42. Rato L, Alves MG, Duarte AI, Santos MS, Moreira PI, Cavaco JE, et al. Testosterone deficiency induced by progressive stages of diabetes mellitus impairs glucose metabolism and favors glycogenesis in mature rat Sertoli cells. The International Journal of Biochemistry & Cell Biology. 2015;66:1–10.
43. Saraswati, P. A. I. ., Gunawan, I. M. K., & Budiyasa, D. G. A. (2021). Overview of glomerulus filtration in type 2 of diabetes mellitus at Sanjiwani Gianyar hospital year of 2018-2019. *International Journal of Health & Medical Sciences*, *4*(1), 50-55. https://doi.org/10.31295/ijhms.v4n1.726
44. Slowinska-Solnica K, Pawlica-Gosiewska D, Gawlik K, Kuzniewski M, Maziarz B, Solnica B. Boronate affinity chromatography accurately measures hba1c also in patients with end-stage renal disease - performance evaluation of the A1C HPLC analyzer. Clinical Laboratory. 2018;64(09/2018).
45. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Health and treatment of diabetes mellitus. *International Journal of Health Sciences*, *5*(1), i-v. https://doi.org/10.53730/ijhs.v5n1.2864
46. Swerdloff RS, Dudley RE, Page ST, Wang C, Salameh WA. Dihydrotestosterone: Biochemistry, physiology, and clinical implications of elevated blood levels. Endocrine Reviews. 2017;38(3):220–54.
47. Vandenput L, Mellström D, Lorentzon M, Swanson C, Karlsson MK, Brandberg J, et al. Androgens and glucuronidated androgen metabolites are associated with metabolic risk factors in men. J Clin Endocrinol Metab

[Internet]. 2007;92(11):4130–7. Available from: http://dx.doi.org/10.1210/jc.2007-0252.
48. Westfield G, Kaiser UB, Lamb DJ, Ramasamy R. Short-acting testosterone: More physiologic? Frontiers in Endocrinology. 2020;11.
49. Yao Q-ming, Wang B, An X-fei, Zhang J-an, Ding L. Testosterone level and risk of type 2 diabetes in men: A systematic review and meta-analysis. Endocrine Connections. 2018;7(1):220–31.