How to Cite:
Jheetay, S., Garg, R., Adhana, R., Kumar, J., Muniyal, H., Verma, A., & Jaura, J. (2022). The utilisation of cardiac risk ratio and non-HDL cholesterol markers to assess cardiovascular risk in type 2 diabetes males with lowered serum DHT. *International Journal of Health Sciences*, *6*(7), 321–337. https://doi.org/10.53730/ijhs.v6n7.10954

The utilisation of cardiac risk ratio and non-HDL cholesterol markers to assess cardiovascular risk in type 2 diabetes males with lowered serum DHT

Sanket Jheetay
PhD Scholar, Department of Physiology, Santosh Deemed to be University, Ghaziabad, U.P and PhD Scholar, Department of Physiology,Santosh Medical College, Ghaziabad, UP 9568397681.
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.

Anjali Verma
Associate Professor, Department of Physiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, U.P.

Jaspreet Jaura
Assistant Professor, Department of Physiology, Teerthanker Mahaveer Medical College & Research Centre, Moradabad, U.P.

***Abstract*---**Background A risk factor for cardiovascular disease, particularly vascular disease when linked to Diabetes Mellitus, is the decline of male sex androgens. In recent years, many forms of studies have been conducted to confirm its link. Male hypogonadism is linked to dyslipidemia, visceral obesity, and CVD disorders. Testosterone's

Manuscript submitted: 9 March 2022, Manuscript revised: 18 May 2022, Accepted for publication: 27 June 2022

role in Type 2 Diabetes has been researched alone or in conjunction with Sex hormone binding globulin. DHT, the most recent androgen to be discovered whose functions are being researched and elaborated upon, hasn't received much attention. Very little research has been conducted in India and Asia that looked at androgens associations with cardiac risk indicators. Methods: The study was carried out at Teerthanker Mahaveer Medical College and Research Centre's Department of Physiology and Medicine and Santosh Medical College's Department of Physiology in Moradabad and Ghaziabad, respectively. A total of 210 samples, including 105 from type 2 diabetes and 105 from controls, were used in the investigation. Lipid parameters [HDL, LDL, VLDL & TC], serum DHT, and data analysis were performed using the conventional biochemical methods and SPSS 26 (trial version). Non-HDL cholesterol was estimated as Total Cholesterol-HDL, and the Cardiac Risk Ratio (CRR) was determined by Total Cholesterol/HDL. Results: Diabetic cases had considerably lower serum levels of dihydrotestosterone than healthy controls [439.26±257.87pg/ml vs 230.66±182.02pg/ml, p=0.001]. Compared to merely 10% of controls, Type 2 diabetics were found to have levels that were 90% below normal. 15 of the 105 patients in the study were obese and related to diabetes and had a BMI > 30. The average BMI for diabetics was 26.99±3.01. Patients with normal DHT levels had significantly higher mean HDL values [49.02±7.93 mg/dl], but those with low DHT levels had lower HDL levels [37.50±14.76 mg/dl] in adults with diabetes. High VLDL, TG, and TC readings were correlated with low DHT levels similarly. In diabetic cases, the Cardiac Risk ratio was 4.89± 1.55 and Non-HDL Cholesterol was 168.75±45.58 mg/dl, whereas in controls, the Cardiac Risk ratio was 3.27 ±1.03 and Non-HDL Cholesterol was 112.6± 35.14 mg/dl. In diabetic cases, DHT had a substantial correlation with Cardiac Risk ratio & Non-HDL Cholesterol, while no significance was seen in the case of controls. Except HDL, which demonstrated a negative association, the cardiac risk ratio had a positive significant relation with lipid parameters. Except for HDL, which demonstrated a non-significant negative association, non-HDL cholesterol and lipid parameters correlated positively and significantly. Conclusion: Males with Type 2 diabetes had significantly reduced DHT levels, with high Lipid parameters and high cardiac risk ratio and high Non-HDL Cholesterol levels.

***Keywords*--**Dihydrotestosterone, type 2 diabetes mellitus, lipid profile, BMI, cardiac risk ratio, non-HDL cholesterol, cardiovascular disease.

Introduction

Despite making major efforts over the past decades, assessing coronary heart disease (CHD) risk in asymptomatic populations remains poor, with higher levels of LDL cholesterol, total cholesterol, and triglycerides in diabetes, but lower levels of HDL cholesterol were seen. [1]This range of altered parameters in adults has been linked to deaths around the world on various continents with micro and

macrovascular complications.[2] Since LDL cholesterol measurement alone is insufficient for risk identification, low-density lipoprotein (LDL) cholesterol concentration has been the primary source of cardiovascular disease risk and the main focus of intervention. [1,2]Although some studies continue to link LDL-C to CVD, the connection was modest, and LDL-C was not a reliable indicator of Death from coronary heart disease.[1] LDL-C and HDL-C levels are thus left for the clinician to use in determining risk when taking into account the occurrence of other significant risk factors, such as gender, nicotine consumption, blood pressure, diabetes, sedentary behaviour, and adiposity.[1,2,3] To enhance the prediction of cardiovascular disease, efforts have been made to identify emerging or novel cardiovascular risk factors. Since lipoprotein ratios like TC/HDL-C, LDL-C/HDL-C, TC-HDL/HDL, and TC-HDL can enhance risk assessment but are underutilised in cardiovascular prevention.[3,4,5] The production of nitric oxide, endothelial proliferation, growth, as well as the inhibition of endothelial inflammation, are all induced by androgens at the blood vessel level, which would thus lower the risk of atherosclerosis. Studies demonstrate a protective role of the cardiovascular system with reduced lipid accumulation in tunica media, vasodilatation, lowering serum cholesterol, TNF-alpha & favourable changes in cardiac muscles. The role and association of DHT having cardioprotective effects are yet to be elaborated on in studies. [6,7] With various studies pointing to its favourable effects, its linkage with risk factors of recent parameters has not been studied. Reliable measures of serum DHT have not yet been made, and the physiological relevance of this hormone has received scant attention and remains uncertain. As a result, the purpose of this study is to evaluate the cardiovascular risk, and non-HDL cholesterol along with an association between DHT and these calculated risk factors. Conclusion: Males with Type 2 diabetes had significantly reduced DHT levels, with high Lipid parameters and high cardiac risk ratio and high Non-HDL Cholesterol levels.

Method

Material and methods:
Selection of study group
Once the ethics committee had given its approval, all 105 male participants in this study who were diagnosed with Type 2 DM (according to WHO criteria FBS > 126 mg/dl and HbA1c > 6.5 per cent)[8] and 105 healthy men who were chosen as controls were over the age of 30 and under 60 years.

Study setup

This research was done at Teerthanker Mahaveer Medical College and Research Centre, Moradabad, in the departments of Physiology, Medicine and the Department of Physiology 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 made up the study's participants. The study didn't include people who were receiving

finasteride, epristeride, saw palmetto extract, or other DHT inhibitors; they also didn't include people who were being treated for benign prostatic hyperplasia or prostate cancer; had liver ailments, had a history of chronic alcoholism or used tobacco & alcohol.[9,10]

Sample size
The sample, which was based on the predicted prevalence of DM type 2 in Western Uttar Pradesh, consisted of 105 diabetic patients and 105 controls (Moradabad).

Estimation methods:

1. Serum glucose estimation by GOD POD Method. [11]
2. Estimation of HbA1c using Boronate Affinity Chromatography. [12]
3. Determination of total cholesterol by CHOD PAP Method. [13]
4. Determination of serum triglycerides by Glycerol oxidase- Trinder method, endpoint method. [14]
5. Determination of HDL-Cholesterol by Modified polyethene glycol precipitation method. [15]
6. Serum LDL-Cholesterol was calculated by Friedwald's formula. [16]
7. Estimation of Serum Dihydrotestosterone levels by using Enzyme-Linked Immunosorbent Assay(ELISA). [17]
8. Atherogenic coefficient (Ac) was computed as TC-HDL/HDL, while cardiac risk ratio (CRR) was determined as TC/HDL.[2]

Data management and analysis plan

The statistical analyses were performed using SPSS version 26(Trial). The descriptive results were expressed as mean ± standard & correlation.

Results

Table 1
Age distribution of study participants

	DIABETIC CASES [n=105]	CONTROL [n=105]	**Total**
Age group (years)	N	N	N
31-40	17	22	39
41 – 50	29	40	69
51 – 60	59	43	102
Total	5	105	210
Mean	49.84±7.88	47.79±7.55	48.81±7.74

The age distribution of the research participants is shown in Table 1. The majority of the diabetic patients in this study were between the ages of 51 and 60 years.

Table 2
Distribution of study population according to BMI

Parameters	DIABETIC CASES [n=105]	CONTROLS [n=105]	Total
BMI Range	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

A body mass index analysis of 57 diabetes cases revealed in Table2, that the majority of the patients (n=57) had an overweight BMI of 25 to 29.99. 15 of the 105 samples were labelled as obese if their BMI was 30 or greater. Diabetics had an average BMI of 26.99± 3.01. However, the bulk of samples (n=84) in the control group had BMIs between 18 and 24.99; their mean BMI was instead 23.78±2.41.

Table 3
Comparison of lipid parameters between Diabetic cases and controls.

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

The mean value of the lipid parameters evaluated in the current study is displayed in Table 3. The levels of LDL, VLDL, triglycerides, and total cholesterol were markedly higher in diabetic patients. In diabetic cases, the HDL was 45.94 ±11.35 mg/dl, compared to 52.83± 9.38 mg/dl in the control group. (p .001). Those with diabetes had LDL levels of 139.24± 45.46 mg/dl compared to 105 ±37.19 mg/dl in the control group. The VLDL levels in the diabetic cases and control group were 29.41 mg/dl and 38.27 mg/dl, respectively. Those with diabetes had triglycerides of 191.34± 56.66 mg/dl compared to 147.05± 78.21 mg/dl in the control group. In diabetic cases, total cholesterol levels were 223.45±49.46 mg/dl and the control groups were 187.49±40.93 mg/dl, respectively.

Table 4
Comparison of serum levels of Dihydrotestosterone between diabetic cases and controls.

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

The DHT in the control group was 439.26 ±257.87 pg/ml, which was a lot higher than in samples without diabetes (p 0.001). In diabetic patients, the DHT level was 230.66 ±182.02 pg/ml.

Table 5
Correlation of dht with cardiac risk ratio & calculated non-hdl cholesterol among diabetic cases

PARAMETERS	Mean±SD	r-value	p-value
Cardiac Risk ratio	4.89±1.55	-.551	<.001
Non-HDL Cholesterol(mg/dl)	168.75±45.58	-.402	<.001

Table 5 denotes the correlation of DHT serum levels with cardiac risk and calculated Non-HDL levels in the plasma of Diabetic cases where the Mean±SD of Cardiac Risk ratio was estimated to be 4.89±1.55, a negative correlation was observed when between DHT levels and Cardiac Risk ratio(r=-0.551) which was highly significant. In the case of Non-HDL Cholesterol, the Mean±SD was 168.75±45.58 mg/dl, which again was a significant correlation of (r= -0.402).

Table 6
Correlation of dht with cardiac risk ratio & non-hdl cholesterol among controls

PARAMETERS	Mean±SD	r-value	p-value
Cardiac Risk ratio	3.27±1.03	-.073	.461
Non-HDL Cholesterol(mg/dl)	112.6±35.14	.043	.665

Table 6 shows the relationship between DHT and the cardiac risk ratio and Non-HDL cholesterol in healthy subjects, Cardiac Risk ratio had a Mean±SD value of 3.27±1.03, although a negative correlation was observed, significance was not seen(r = -0.073). In the case of calculated Non-HDL Cholesterol, Mean±SD in controls was 112.6 ±35.14 mg/dl with no significance in correlation (r=0.043).

Table 7
Correlation of cardiac risk ratio with lipid parameters among diabetic cases

PARAMETERS	Mean±SD	r-value	p-value
HDL (mg/dl)	45.94±11.35	-.741	<.001
LDL(mg/dl)	139.24±45.46	.573	<.001
VLDL(mg/dl)	38.27±11.33	.544	<.001
TRIGLYCERIDES (mg/dl)	191.34±56.66	.545	<.001
TOTAL CHOLESTEROL (mg/dl)	223.45±187.49	.495	<.001

The correlation between the cardiac risk ratio and lipid parameters among diabetic cases is seen in Table 7. HDL was negatively correlated with a Cardiac risk ratio (r= -0.741) which was highly significant, LDL, VLDL, Triglycerides & Total Cholesterol had a positive correlation, r = 0.573,r =0.544, r= 0.545, & r= 0.495 respectively. All the lipid parameters HDL, LDL, VLDL, Triglycerides & Total Cholesterol correlation were highly significant.

Table 8
Correlation of calculated non-hdl cholesterol with lipid parameters among diabetic cases

PARAMETERS	Mean±SD	r-value	p-value
HDL(mg/dl)	45.94±11.35	-.076	.441
LDL(mg/dl)	139.24±45.46	.970	<.001
VLDL(mg/dl)	38.27±11.33	.386	<.001
TRIGLYCERIDES (mg/dl)	191.34±56.66	.387	<.001
TOTAL CHOLESTEROL (mg/dl)	223.45±187.49	.974	<.001

Table 8 shows a correlation between calculated non-HDL cholesterol and lipid parameters in diabetic cases, HDL although having a negative correlation with Non-HDL cholesterol was non-significant. LDL, VLDL, Triglycerides & Total Cholesterol had a positive correlation with a high significance(r = .970, r = .386,r= .387, r = .974 respectively).

Discussion

The predominant sex hormone for men is testosterone, which is changed into the metabolites dihydrotestosterone and oestrogen. In older and middle-aged men, lower levels of the hormones testosterone and dihydrotestosterone are linked to greater cardiovascular deaths.[18] Androgens promote endothelium development, proliferation, and nitric oxide release during vascular injury healing. As a result, there is an increase in cGMP synthesis, which causes hyperpolarization and vasodilation.[19,20] additionally a lower release of inflammatory mediators cytokines, lowering the apoptosis of endothelial cells. [21]

BMI is a rather fundamental indicator of metabolic risk. Studies that use the body mass index (BMI, kg/m2) as a gauge of the accumulation of additional fat mass have discovered a variety of connections between CVD mortality and BMI.[22,23] Similarly important marker for mortality has been waist circumference, after the conclusion of a typical expiration, the waist circumference is measured at the lowest waist level or the 12th rib.[24] Compared to lesser correlations for BMI and waist to hip ratio, waist circumference consistently showed the strongest link with mortality risk for various factors in some studies.[24] Some research also recommends using the waist-to-hip ratio rather than BMI to assess a patient's risk of CVD. Increases in the waist-to-hip ratio were also shown to be linked to an increased risk of coronary heart disease.[25] When compared to subcutaneous fat, visceral fat tissue is more closely associated with cardiovascular events. This is supported by studies that suggest certain people, even those with BMIs in the obese range, may well have robust metabolisms due to decreased visceral fat tissue levels. On the other hand, some individuals with BMIs within the normal limits may exhibit a collection of obesity-related risk factors for diabetes and cardiovascular disease. At various junctions, studies have relied on BMI, waist-hip circumference and some on waist-hip ratio etc where one was considered a better marker over the other.[26]

LDL cholesterol measure, heavily relied upon is insufficient to assess the atherogenic risk in patients with hypertriglyceridemia and diabetes, and the use of a secondary indicator or many others are recommended.[27] According to the evidence, LDL-C had a marginal relationship with cardiovascular disease (CVD) and was not a reliable indicator of mortality from coronary heart disease (CHD).[28] Table 1 displays the age distribution of the study participants. In this study, the bulk of the diabetes cases ranged in the age group from 51 to 60 years. 15 of the 105 samples were classified as obese, their BMI was 30 or higher.

A BMI of diabetic subjects (n=57) found that the majority of the subjects (n=57) were under the category of overweight BMI(25 to 29.99). The average BMI for diabetics was 26.99± 3.01. The majority of samples (n=84) in the control group, on the other hand, had BMIs between 18 and 24.99; their mean BMI was instead 23.78± 2.41. Studies were done in India where similar results of BMI were seen in the case of Diabetics with the majority in the Obese and overweight category.[29,30] The most significant risk factor for developing hyperglycemia in India was high BMI, Between 1990 and 2016, there was a rise in every state of India in the prevalence of overweight among individuals aged 20 or older. This rise is caused by the substitution of staple foods for energy-dense, high-carbohydrate diets, the

rise of idle jobs, and the decline in physical activity levels brought on by urbanized and financial changes.[31]

Table 3 shows the mean value of the lipid parameters assessed in the current investigation. In diabetic patients, LDL, VLDL, triglycerides, and total cholesterol levels were significantly higher. The HDL level in diabetic cases was 45.94± 11.35 mg/dl versus 52.83 ±9.38 mg/dl in the control group. (p .001). LDL values were 139.24± 45.46 mg/dl in those with diabetes against 105± 37.19 mg/dl in the control group. Diabetes causes and the control group had VLDL values of 29.41 mg/dl and 38.27 mg/dl, respectively. Triglycerides were 191.34± 56.66 mg/dl in those with diabetes against 147.05± 78.21 mg/dl in the control group. Total cholesterol levels were 223.45±49.46 mg/dl in diabetes cases and 187.49±40.93 mg/dl in the control groups, respectively.

Both male and female type 2 diabetic patients had a prevalence of dyslipidemia of 85% in a study, with males having a prevalence of 86 per cent. In a different study, patients with type 2 diabetes who had dyslipidemia had a 90% prevalence rate. In light of the emergence of cardiovascular or cerebrovascular disorders, these lipid abnormalities may be significant. based on the above research, there is an 80–90% chance that Type 2 Diabetes will have dyslipidemia.[32-34]

The DHT in the control group was much greater than in those without diabetes, resulting in 439.26± 257.87 pg/ml (p 0.001). DHT levels in diabetes individuals were 230.66 ±182.02 pg/ml. Low DHT levels were found to be directly associated with increased insulin resistance and a higher risk of diabetes in research by Joyce et al. on older males. They noted that levels of DHT in older males were strongly linked to a lower risk of diabetes and lesser insulin resistance.[35] Research conducted by Mather et al. in their study discovered that DHT was related to postprandial blood glucose levels, inverse fasting insulin, and the insulinogenic index in addition to fasting blood glucose levels. They discovered a relationship between BMI & waist circumference in addition to glycemic indices.[36] In older males, insulin resistance and fat mass were shown to be inversely correlated with DHT levels by Vandenput et al. Testosterone was not associated in the study, however, DHT was independently negatively associated. Vandenput et al found that in young adult male individuals, DHT and testosterone were both inversely correlated with body weight, BMI, serum leptin, and all measures of total body fat as well as region-specific adipose tissues. [37]

In cases of diabetic cases where the Mean±SD (Table5) of the cardiac risk ratio was estimated to be 4.89±1.55, Table 5 shows the correlation of DHT serum levels with cardiac risk and calculated Non-HDL levels. A negative correlation between DHT levels and the cardiac risk ratio was found (r=-0.551), which was highly significant. Non-HDL cholesterol had a mean and standard deviation of 168.75±45.58 mg/dl, which again indicated a significant association (r= -0.402). In control subjects, the cardiac risk ratio had a Mean±SD value of 3.27±1.03 and a relationship between DHT and Non-HDL cholesterol was shown in Table 6. Although a negative correlation was seen, significance was not seen in their association (r = -0.073). Measured Non-HDL Cholesterol in controls was 112.6± 35.14 mg/dl with no statistically significant correlation (r = 0.043). Table 7 shows the relationship between the cardiac risk ratio and lipid variables in diabetic

subjects. LDL, VLDL, Triglycerides, and Total Cholesterol had positive correlations with r= 0.573, r= .544, r= .545, and r= .495, respectively, but HDL had a negative correlation with a cardiac risk ratio (r= -0.741), which was highly significant.

Table 8 illustrates a relationship between calculated non-HDL cholesterol and lipid parameters in diabetic cases, HDL, despite having a negative relationship with non-HDL cholesterol, was not statistically significant. The connection between LDL, VLDL, Triglycerides and Total Cholesterol was positive and highly significant (r = 0.970, 0.386,0.387, and 0.974, respectively). With a diagnostic value on par with measuring total cholesterol, Cardiac Risk Ratio (CRR) reflects the development of coronary plaques, since CRR shows the change in the vasculature of coronary vessels.[38] Compared to total cholesterol, CRR is a more sensitive and specific indicator of cardiovascular risk, especially in people with triglycerides greater than 300 mg/dl. [39] The long-term risk of atherosclerotic cardiovascular disease is substantially correlated with non-HDL cholesterol concentrations in blood. Early-life elevated non-HDL cholesterol blood concentrations are prognostic of incident cardiovascular disease and appear to remain stable throughout life. In the 2516 participants of the Framingham Offspring Study, non-HDL cholesterol testing revealed that constant amounts throughout a lifetime may be associated with an elevated risk of cardiovascular disease.[30,31]

A higher DHT level was associated with reduced IHD mortality according to Yeap et al. plasma DHT above the median value (39 ng/dL) was associated with lower IHD mortality risk. Their findings also suggested higher DHT was associated with reduced IHD mortality but not with non-IHD mortality, affirming the fact that androgens are protective against IHD. Similar findings in our study are observed where Diabetics had higher value of Lipid parameters when compared to that controls. Diabetics displayed lower DHT values, with high lipid profiles which are per the study.[32] As described above Mather et al. had shown a negative correlation of DHT with BMI, waist circumference & glycaemic parameters which are important factors for the development of cardiac disease risk factors in males. [36] In ageing males, DHT may increase longevity or lower the risk of CVD events. Serum DHT may affect CVD risk through vascular changes, platelets, and inflammatory processes.[7,33] Wu and von Eckardstein, (2003) & a study by Norata et al. (2006) reported Dihydrotestosterone was found to be able to reduce the inflammatory response generated by a lipopolysaccharide-induced inflammatory response and TNF-alpha in human endothelial cells of blood vessels, whereas androgens increase coronary artery vasodilatation and promote myocardial function. For instance, testosterone or its metabolite DHT reduces the tone of the coronary arteries, which thereby increases myocardial perfusion.[33,34] With a value higher than the cutoff risk level (<130mg/dl) of no-HDL cholesterol & Cardiac risk ratio(<3.5:1) in diabetics with low DHT serum levels, the chances of cardiovascular disease increase, high apolipoprotein levels & added pathogenesis as above tend to occur.[35,36,37,38] According to the research findings mentioned above, higher DHT levels are associated with lower IHD mortality, which is consistent with a possible cardioprotective action of DHT. Markers such as Cardiac Risk ratio and Non- HDL Cholesterol have a higher value in the case of Diabetics than Controls, both of which signify a high risk of cardiovascular diseases, associated with low serum DHT signifies the importance of androgens,

especially DHT. Future studies and clinical trials are necessary to ascertain its prognostic value, including randomised trials of testosterone and DHT, and to ascertain whether interventions that change the levels of testosterone or DHT in serum can increase life expectancy or reduce the risk of developing cardiovascular disease (CVD) events. Although a larger sample size, added sex hormones and follow-up would further strengthen the study and are the limitations of the study. These will then result in emphasising the significance of DHT in addition to testosterone for its cardioprotective effects.

Conclusion

As per this study, DHT levels were noticeably lower in males with type 2 diabetes mellitus than in controls, and this difference was highly significant. Patients with type 2 diabetes mellitus had significantly higher levels of lipid parameters (total cholesterol, LDL, VLDL, and triglycerides), whereas HDL levels were low in diabetic individuals. DHT serum levels were low in Diabetics than in controls, having a negative correlation with Cardiac risk ratio & Non-HDL Cholesterol in Diabetic cases. No correlation was observed between DHT with Cardiac risk ratio & Non-HDL Cholesterol in control samples. Cardiac risk ratio & Non-HDL Cholesterol calculated values were higher in the case of Diabetic cases and lower in controls cardiac Risk ratio and lipid parameters in diabetic cases were shown to be significantly correlated, Non-HDL cholesterol and lipid parameters in diabetic cases were also found to be significantly related. All these findings hence conclude the fact that lower serum DHT levels in type 2 diabetes are associated with a higher predisposition to atherosclerotic events, as there is a high possibility of coronary plaque formation. Maintenance of the physiological range of DHT and Testosterone through diet, exercise and lifestyle modifications along with the treatment regimen in males could lead to lower lipid parameter alterations and lower chances of plaque formation in coronary vessels. Hence preventing Ischemic events in the heart, and low chances of mortality as the decline of DHT decline has been directly linked to CVD-related deaths.

References

1. Jamor P, Ahmadvand H, Birjandi M, Ebadi Sharafabad B. Activity of serum paraoxonase 1, lipid profile and atherogenic indexes in diabetic induced rats treated with alpha lipoic acid. Journal of Nephropathology. 2018;7(4):241–7.
2. Ukwamedu HA AEM. Assessment of cardiovascular risk indices in type 2 diabetes mellitus. Tropical Medicine & Surgery. 2015;03(02).
3. Lemieux I, Lamarche B, Couillard C, Pascot A, Cantin B, Bergeron J, et al. Total cholesterol/HDL cholesterol ratio vs LDL cholesterol/HDL cholesterol ratio as indices of ischemic heart disease risk in men. Archives of Internal Medicine. 2001;161(22):2685.
4. Manninen V, Tenkanen L, Koskinen P, Huttunen JK, Mänttäri M, Heinonen OP, et al. Joint effects of serum triglyceride and LDL cholesterol and HDL cholesterol concentrations on coronary heart disease risk in the Helsinki Heart Study. implications for treatment. Circulation. 1992;85(1):37–45.

5. Lamarche B, Moorjani S, Lupien PJ, Cantin B, Bernard P-M, Dagenais GR, et al. Apolipoprotein A-I and B levels and the risk of ischemic heart disease during a five-year follow-up of men in the que´bec cardiovascular study. Circulation. 1996;94(3):273–8.
6. Morgentaler A, Miner MM, Caliber M, Guay AT, Khera M, Traish AM. Testosterone therapy and cardiovascular risk: Advances and controversies. Mayo Clinic Proceedings. 2015;90(2):224–51.
7. Chistiakov D, Myasoedova V, Melnichenko A, Grechko A, Orekhov A. Role of androgens in cardiovascular pathology. Vascular Health and Risk Management. 2018;14:283–90.
8. Karnchanasorn, R., Huang, J., Ou, H.-Y., Feng, W., Chuang, L.-M., Chiu, K. C., & Samoa, R. Comparison of the current diagnostic criterion of hba1c with fasting and 2-hour plasma glucose concentration. *Journal of Diabetes Research. 2016*; 1–11. https://doi.org/10.1155/2016/6195494
9. Dhariwala, M. Y., & Ravikumar, P. (2019). An overview of herbal alternatives in androgenetic alopecia. *Journal of Cosmetic Dermatology*. https://doi.org/10.1111/jocd.12930
10. Swerdloff, R. S., Dudley, R. E., Page, S. T., Wang, C., & Salameh, W. A. (2017). Dihydrotestosterone: Biochemistry, physiology, and clinical implications of elevated blood levels. *Endocrine Reviews*, *38*(3), 220–254. https://doi.org/10.1210/er.2016-1067 .
11. 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.
12. 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).
13. Biotec-co.com. [cited 2022 Jun 30]. Available from: https://www.biotec-co.com/images/products/clinical_chemistry/kits/chemistry/Cholesterol.pdf
14. Adveetabiotech.com. [cited 2022 Jun 30]. Available from: https://adveetabiotech.com/wp-content/uploads/2020/05/21_Triglycerides-_Test_Kit.pdf
15. 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
16. 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.
17. 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.
18. U.S. National Library of Medicine. (n.d.). *Home - books - NCBI*. National Center for Biotechnology Information. Retrieved July 12, 2022, from https://www.ncbi.nlm.nih.gov/books

19. Wynne, F. L., & Khalil, R. A. (2003). Testosterone and coronary vascular tone: Implications in coronary artery disease. *Journal of Endocrinological Investigation*, *26*(2), 181–186. https://doi.org/10.1007/bf03345150
20. Marrachelli, V. G., Miranda, F. J., Centeno, J. M., Salom, J. B., Torregrosa, G., Jover-Mengual, T., Pérez, A. M., Moro, M. A., & Alborch, E. (2010). Role of no-synthases and cyclooxygenases in the hyperreactivity of male rabbit carotid artery to testosterone under experimental diabetes. *Pharmacological Research*, *61*(1), 62–70. https://doi.org/10.1016/j.phrs.2009.06.008
21. Norata, G. D., Tibolla, G., Seccomandi, P. M., Poletti, A., & Catapano, A. L. (2006). Dihydrotestosterone decreases tumor necrosis factor-α and lipopolysaccharide-induced inflammatory response in human endothelial cells. *The Journal of Clinical Endocrinology & Metabolism*, *91*(2), 546–554. https://doi.org/10.1210/jc.2005-1664
22. Khan SS, Ning H, Wilkins JT, Allen N, Carnethon M, Berry JD, et al. Association of Body Mass index with lifetime risk of cardiovascular disease and compression of morbidity. JAMA Cardiology. 2018;3(4):280–7.
23. Zhao Y, Qie R, Han M, Huang S, Wu X, Zhang Y, et al. Association of BMI with cardiovascular disease incidence and mortality in patients with type 2 diabetes mellitus: A systematic review and dose–response meta-analysis of Cohort studies. Nutrition, Metabolism and Cardiovascular Diseases. 2021;31(7):1976–84.
24. Peters SA, Bots SH, Woodward M. Sex differences in the association between measures of general and central adiposity and the risk of myocardial infarction: Results from the UK Biobank. Journal of the American Heart Association. 2018;7(5).
25. Murray S. Is waist-to-hip ratio a better marker of cardiovascular risk than body mass index? Canadian Medical Association Journal. 2006;174(3):308–.
26. Gruzdeva O, Borodkina D, Uchasova E, Dyleva Y, Barbarash O. Localization of fat depots and cardiovascular risk. Lipids in Health and Disease. 2018;17(1):218.
27. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. Circulation. 2002;106(25):3143-3143.
28. Lehto S, Rönnemaa T, Pyörälä K, Laakso M. Cardiovascular risk factors clustering with endogenous hyperinsulinaemia predict death from coronary heart disease in patients with Type II diabetes. Diabetologia. 2000;43(2):148-155.
29. Vasanthakumar J, Kambar S. Prevalence of obesity among type 2 diabetes mellitus patients in urban areas of Belagavi. Indian Journal of Health Sciences and Biomedical Research (KLEU). 2020;13(1):21.
30. Unnikrishnan A, Kalyan M, Dhore P, Purandare V, Deshpande S. Obesity and its link to undiagnosed diabetes mellitus and hypertension in rural parts of western India. Indian Journal of Endocrinology and Metabolism. 2020;24(2):155.
31. Tandon N, Anjana R, Mohan V, Kaur T, Afshin A, Ong K et al. The increasing burden of diabetes and variations among the states of India: the Global Burden of Disease Study 1990–2016. The Lancet Global Health. 2018;6(12):e1352-e1362.

32. Pandya H, Lakhani JD, Dadhania J, Trivedi A. The prevalence and pattern of dyslipidemia among type 2 diabetic patients at rural based hospital in Gujarat, India. Indian J Clinic Pract. 2012;22(12):36-44.
33. Tagoe DN, Amo-Kodieh P. Type 2 diabetes mellitus influences lipid profile of diabetic patients. Annals Bio Res. 2013;4(6):88-92.
34. Jayarama N, Reddy M, Raj SD. Prevalence and pattern of dyslipidemia in type 2 diabetes mellitus patients in a rural tertiary care centre, southern India. Glob J Med Public Health. 2012;1:24-8.
35. Joyce K, Biggs M, Djoussé L, Ix J, Kizer J, Siscovick D 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;:jc.2016-2623.
36. Mather K, Kim C, Christophi C, Aroda V, Knowler W, Edelstein S et al. Steroid Sex Hormones, Sex Hormone–Binding Globulin, and Diabetes Incidence in the Diabetes Prevention Program. The Journal of Clinical Endocrinology & Metabolism. 2015;100(10):3778-3786.
37. Vandenput L, Mellström D, Lorentzon M, Swanson C, Karlsson M, Brandberg J et al. Androgens and Glucuronidated Androgen Metabolites Are Associated with Metabolic Risk Factors in Men. The Journal of Clinical Endocrinology & Metabolism. 2007;92(11):4130-4137.
38. Salcedo-Cifuentes M, Belalcazar S, Acosta E, Medina-Murillo J. Conventional biomarkers for cardiovascular risks and their correlation with the castelli risk index-indices and tg/hdl-c. Archivos de Medicina (Manizales). 2019;20(1):11-22.
39. Genest J, Frohlich J, Fodor G, McPherson R; Working Group on Hypercholesterolemia and Other Dyslipidemias. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: summary of the 2003 update. CMAJ; 2003;169(9):921-924.
40. Brunner F, Waldeyer C, Ojeda F, Salomaa V, Kee F, Sans S et al. Application of non-HDL cholesterol for population-based cardiovascular risk stratification: results from the Multinational Cardiovascular Risk Consortium. The Lancet. 2019;394(10215):2173-2183.
31. Pencina K, Thanassoulis G, Wilkins J, Vasan R, Navar A, Peterson E et al. Trajectories of Non–HDL Cholesterol Across Midlife. Journal of the American College of Cardiology. 2019;74(1):70-79.
32. Yeap B, Alfonso H, Chubb S, Handelsman D, Hankey G, Almeida O et al. In Older Men an Optimal Plasma Testosterone Is Associated With Reduced All-Cause Mortality and Higher Dihydrotestosterone With Reduced Ischemic Heart Disease Mortality, While Estradiol Levels Do Not Predict Mortality. The Journal of Clinical Endocrinology & Metabolism. 2014;99(1):E9-E18.
33. Wu F, von Eckardstein A. Androgens and Coronary Artery Disease. Endocrine Reviews. 2003;24(2):183-217.
34. Norata G, Tibolla G, Seccomandi P, Poletti A, Catapano A. Tu-P7:120 Dihydrotestosterone decreases tumor necrosis factor A and lipopolysaccharide induced inflammatory response in human endothelial cells. Atherosclerosis Supplements. 2006;7(3):211.
35. Su X, Kong Y, Peng D. Evidence for changing lipid management strategy to focus on non-high density lipoprotein cholesterol. Lipids in Health and Disease. 2019;18(1).

36. Bittner V, Bertolet M, Barraza Felix R, Farkouh M, Goldberg S, Ramanathan K et al. Comprehensive Cardiovascular Risk Factor Control Improves Survival. Journal of the American College of Cardiology. 2015;66(7):765-773.
37. Biochemistry, high density lipoprotein - NCBI bookshelf [Internet]. StatPearls. [cited 2022Jul16]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549802/
38. Making sense of cholesterol tests [Internet]. Harvard Health. 2022 [cited 2022Jul16]. Available from: https://www.health.harvard.edu/heart-health/making-sense-of-cholesterol-tests
39. 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