Correlation between anthropometric indices and dyslipidemia in T2DM: CHD risk assessment and identification of Metabolic Syndrome.

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Abstract:

Introduction: Anthropometric indices and dyslipidemia have been associated with Type 2 Diabetes Mellitus (T2DM). **Objective:** Present study aimed at examining these variables in the North Indian rural population of Sirmaur District of Himachal Pradesh, India. **Materials & Methods:** In a cross-sectional and case control study, age-sex matched controls for clinically established patients were enrolled. Data based upon demographic, anthropometric and biochemical variables were collected. Student's *t*-test and Pearson's correlation analyses were performed on the data with SPSS v16.0. Following the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III guidelines, Coronary Heart Disease (CHD) risk evaluation and the identification of Metabolic Syndrome in the enrolled patients was conducted. **Results:** All the variables showed significantly (p=0.000) higher values in case of patients than the controls. On subjecting to correlation analysis, while the poor glycemic control, higher anthropometric indices and urea showed significant (p=0.000) correlation to elevated fasting blood sugar, it was unrelated to lipid profile but, dyslipidemia and higher anthropometric indices were strongly correlated. Men were at higher risk of CHD (10 year risk equivalent) as compared to women. Higher number of men (88%) had metabolic syndrome (MetS) than women (80%). **Conclusion:** The study helps draw conclusion that anthropometric indices are good predictors of T2DM and silent dyslipidemia is observed in such patients. More significantly, T2DM does influence the overall health of an individual with particular impact on the risk factors associated with CHD. Timely intervention with life style changes and drugs and constant monitoring can help alleviate the risk factors and reduce associated complications.

Keywords: Anthropometric indices, CHD risk assessment, Dyslipidemia, Metabolic syndrome, Type 2 Diabetes Mellitus.

Introduction:

A chronic condition characterized by hyperglycemia due to defects in secretion of insulin, insulin action and/or both, acquired and/or inherited, is widely known as diabetes mellitus[1, 2]. The chronic hyperglycemia leads to dysfunction, long term damage and eventual failure of associated organs such as nerves, eyes, kidneys, blood vessels and heart[2]. It is also referred to as type 2 diabetes mellitus (T2DM). The International Diabetes

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Federation (IDF) estimated 72.9 million diabetics amongst Indians in 2017, and projected the number to rise to almost double at 134.3 million by 2045. Urban India, particularly metropolitans, have seen an increase in prevalence of diabetes to over 20% at present from 2% in 1970s. Even the rural areas of India are also catching it up fast[3].It is no secret that India is at present, the Diabetic Capital of the world owing to its mammoth numbers.

There is an extensive amount of literature related to T2DM. Numerous works are available that aim to identify predictors so that the onset can either be delayed or completely avoided or in advanced conditions, might guide us through sustainable management of T2DM. Anthropometric indices have been found to be reliable predictors of T2DM[4, 5, 6]. Some authors have reported that Waist Hip Ratio (WHR) indicating overall obesity is a better predictor[5, 7, 8]. These observations are supported by the findings that insulin resistance is associated with both obesity and more strongly with abdominal obesity[9, 10]. Derangements in anthropometric indices are seen with dyslipidemia which further increases the risk of cardiovascular diseases[11, 12, 13, 14]. Characteristic of insulin resistance, commonly observed as diabetic dyslipidemia, is characterized by high serum triglycerides (TG), low high density lipoproteins (HDL) and changed low density lipoproteins (LDL)[3, 13]. High lipid profile has been found to be associated with poor glycemic control in T2DM patients[15, 16, 17].

The risk factors mentioned above including dyslipidemia, abdominal obesity, hyperglycemia clustered with hypertension are collectively termed as Metabolic Syndrome (MetS), also known as cardiometabolic syndrome or insulin resistance syndrome [18]. Thus, it becomes imperative/natural to study MetS during T2DM.It remains a universal understanding that all these factors also contribute to coronary heart disease (CHD).

In this study, the work was designed with clinically established T2DM patients visiting Dr. Yashwant Singh Parmar Govt. Medical College & Hospital, Nahan, Himachal Pradesh, India. Demographic, anthropometric indices and biochemical parameters were examined in a case – control study. Further, probable association between CHD risk and MetS was also evaluated.

Objectives of the study:

1. To study the anthropometric and biochemical parameters of T2DM patients of rural areas of district Sirmaur visiting Dr. Yashwant Singh Parmar Govt. Medical College & Hospital, Nahan, Himachal Pradesh, India.
2. Investigation of a correlation between the variables under study.
3. Evaluation of associated CHD risk and identification of Metabolic Syndrome in these patients.

Materials &Methods:

Consecutive 50 T2DM patients attending diabetic clinic were included in this observational cross-sectional study. Age and sex matched 50 controls were also included in the study. Informed written consent was obtained from every participant and various anthropometric and biochemical investigations were performed based on the predesigned questionnaire.

Height, Weight and Body Mass Index (BMI) based on WHO guidelines for Asia-

Pacific region, were observed. WHR was considered abnormal, if ≥0.95 for males and >0.8 for females[1].Fasting Plasma Glucose (FPG) was defined as plasma glucose after no caloric intake for at least 8 hours. Glycated hemoglobin or hemoglobin A1c (HbA1c) was determined by using commercially available NycoCard HbAlc kit. The biochemical variables were estimated using the standard commercial kits. Very Low Density Lipoproteins (VLDL) were determined by Friedewald equation method.

Statistical analysis was carried out with SPSS version 16.0. A student's *t*-test was performed in order to compare if there was any difference in the values of the variables under study in case of both patients and controls. Pearson's correlation coefficient was calculated in order to check if any of the variables under study had any correlation. This helped to identify the inter-relationship of the variables and if any derailment in the values of a particular variable could be established as a predictor for the other. It is to certify that the study was performed with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments, further adopted by ICMR.

CHD risk assessment and MetS identification:

Adult Treatment Panel-III (ATP-III) guidelines laid by National Cholesterol Education Program (NCEP) of National Institute of Health (NIH) were used to evaluate the CHD risk and there by underlying metabolic syndrome amongst the patients studied[19]. Based on the lipoproteins profiles of a person after 9-12 hour fast, three levels of 10 year risk assessment was suggested based on Framingham tables mentioned. The three levels were>20%, 10-20% and <10% CHD risk assessment. In case if lifestyle interventions and further drugs were not able to control the risk factors, then the person was further evaluated for MetS. A person was considered to have metabolic syndrome if any of the three factors amongst abdominal obesity, TG, HDL, blood pressure (BP) and fasting plasma glucose were higher than cut-off values.

Following were the cut-off values of various variables used to identify metabolic syndrome:

1. Abdominal obesity (Waist circumference)
    a. Women >102 cm (>40 in)
    b. Men >88 cm (>35 in)
2. TG ≥150 mg/dL
3. HDL
    a. Women <40 mg/dL
    b. Men <50 mg/dL
4. Blood pressure ≥130/≥85 mmHg
5. Fasting blood sugar ≥110 mg/dL

In the present study triglycerides, HDL, blood pressure and FPG were used to identify metabolic syndrome.

Results:

Table 1 shows the mean values of demographic, anthropometric and biochemical variables of the population studied. Of the age and sex matched patients and controls, 50% were females and 50% were males. The mean age of patients was 53 yrs. The mean weight of

patients was 64 kg while that of control subjects was 53 kg indicating clearly of underlining health concerns in T2DM. FPG and HbA1c clearly reflect high serum glucose levels and poor glycemic control. The values of urea and creatinine were within the normal range. The biochemical variables on the lipid panel – TG, total cholesterol, HDL, LDL and VLDL, all showed higher values for the patients as compared to corresponding controls.

Table 1. Summary of demographic, anthropometric and biochemical variables of the population under study

Sr. No.	Variable	Mean±S.D.*	
		Patient	Control
1	Age (yrs)	53.20±11.70	51.20±8.98
2	Height (m)	1.68±0.04	1.6386±0.08
3	Weight (kg)	64.12±12.34	53.92±6.30
4	WHR	0.96±0.08	0.83±0.05
5	BMI	22.80±3.64	20.02±0.95
6	FPG (mg/dl)	245.88±69.51	92.50±6.85
7	HbA1c (%)	8.51±1.71	3.18±0.45
8	UREA (mg/dl)	40.92±16.06	29.42±3.77
9	Creatinine (mg/dl)	1.24±0.43	0.85±0.16
10	Triglycerides (mg/dl)	208.60±46.32	142.46±5.94
11	Total Cholesterol (mg/dl)	257.98±67.11	167.46±18.88
12	HDL (mg/dl)	56.18±14.45	36.52±3.09
13	LDL (mg/dl)	160.22±54.56	102.45±19.00
14	VLDL (mg/dl)	41.72±9.29	28.49±1.18

*S.D. = Standard Deviation

Table 2. Table showing *t* and *p* values for variables under study after student's *t*-test between patients and controls.

Sr. No.	Variable	*t*	*p*
1	Age (yrs)	0.958	0.340
2	Height (m)	3.618	0.000*
3	Weight (kg)	5.201	0.000*
4	WHR	8.596	0.000*
5	BMI	5.199	0.000*
6	FPG (mg/dl)	15.526	0.000*
7	HbA1c (%)	21.222	0.000*
8	Urea (mg/dl)	4.929	0.000*
9	Creatinine (mg/dl)	5.870	0.000*
10	TG (mg/dl)	10.014	0.000*
11	Total Cholesterol (mg/dl)	9.180	0.000*
12	HDL (mg/dl)	9.404	0.000*
13	LDL (mg/dl)	7.070	0.000*
14	VLDL (mg/dl)	9.983	0.000*

* Significant at 0.00%

In order to ascertain whether the higher values of the various variables for patients

than controls were significant or not, student's *t*-test was performed. The *t* value for age of patients and controls was 0.958 and was not significant (*p* = 0.340) (Table 2). This ascertained that the population under study was age matched for patients and controls. Whereas comparison of *t* value for patients and controls of various variables under study was significant (p=0.000). This highlighted that the deranged values of various anthropometric and biochemical variables might function as predictors for T2DM. Long term T2DM is known to affect kidney functioning. Although urea and creatinine levels were within normal range yet *t*-test indicated the values for patients were significantly higher as compared to controls.

Correlation amongst various variables:

Table 3. Pearson's correlation coefficient of various variables with FPG, BMI and WHR.

Sr. no.	Variables		FPG	BMI	WHR
1	WHR	PC	-0.074	0.570*	
		P	0.612	0.000	
2	BMI	PC	-0.031		0.570*
		P	0.833		0.000
3	HbA1c	PC	0.683*	-0.002	0.070
		P	0.000	0.989	0.627
4	FPG	PC		-0.31	-0.074
		P		0.833	0.612
5	TG	PC	0.23	0.168	0.064
		P	0.875	0.245	0.660
6	Total Cholesterol	PC	0.190	0.535*	0.369**
		P	0.187	0.000	0.008
7	HDL	PC	0.087	0.472**	0.276
		P	0.546	0.001	0.053
8	LDL	PC	0.194	0.512*	0.381**
		P	0.176	0.000	0.006
9	VLDL	PC	0.022	0.171	0.065
		P	0.882	0.235	0.652
10	Urea	PC	0.392**	0.247	-0.089
		P	0.005	0.084	0.540
11	Creatinine	PC	0.260	0.217	-0.174
		P	0.068	0.129	0.226

PC = Pearson's Coefficient; P = level of significance; * Significant at 0.00%; ** Significant at 0.05%

An establishment of significant difference of the variables between patients and controls warranted further investigation whether these are correlated or not. To determine this, a set of Pearson's correlation analysis was conducted. In one set, correlation between FPG levels (one of the defining criteria for T2DM) and anthropometric variables i.e., WHR and BMI (which are considered predictors of T2DM) with all other variables was studied (Table 3). The FPG levels were directly and significantly correlated to HbA1c and raised urea levels only. There was no correlation amongst FPG and variables on lipid panel. Even the

anthropometric variables were also not correlated with FPG. Total cholesterol (PC=0.535**), HDL (PC=0.472**) and LDL (PC=0.512**) were significantly (p=0.000) correlated to BMI. Whereas only total cholesterol (PC=0.369**) and LDL (PC=0.381**) were significantly (p=0.000) correlated to WHR. There was no correlation amongst triglycerides and VLDL from the lipid panel with blood sugar, BMI or WHR. Amongst the renal function variables studied, only elevation in urea level was significantly (p=0.000) correlated (PC=0.392**) to elevated FPG. However, the serum creatinine level was not correlated with FPG, WHR or BMI.

In case of long term diabetics, some studies have reported dyslipidemia as the predictor for T2DM and is correlated with poor glycemic control. Thus, another set of correlation was studied to investigate if the same held ground for the present population. No correlation was found between HbA1c and any of the variables on the lipid panel. It was however observed that all the variables on the lipid panel – serum TG, total cholesterol, HDL, LDL and VLDL were significantly correlated amongst each other (Table 4).

Table 4. Pearson's correlation coefficient of HbA1c and variables on lipid panel.

Sr. no.	Variables		HbA1c	Total Cholesterol	HDL	LDL	VLDL
1	TG	PC	0.076	0.629*	0.530*	0.468*	1.000*
		P	0.559	0.000	0.000	0.001	0.000
2	Total Cholesterol	PC	0.122		0.641*	0.962*	0.630*
		P	0.339		0.000	0.000	0.000
3	HDL	PC	0.094			0.443*	0.534*
		P	0.518			0.000	0.000
4	LDL	PC	0.099				0.469**
		P	0.495				0.001
5	VLDL	PC	0.078				
		P	0.592				

PC = Pearson's Coefficient; P = level of significance; * Significant at 0.00%; ** Significant at 0.05%

Evaluation of CHD risk equivalent:

Table 5. Coronary heart disease (10 year) risk equivalent amongst patients

Sr. No.	% of risk factor (10 year)	Women (no.)	Men (no. /%age)
1	>20% CHD risk equivalent	-	-
2	10-20% CHD risk equivalent	-	14 (56%)
3	<10% CHD risk equivalent	25	11 (44%)

Details of CHD risk factor equivalent for patients under study is provided in Table 5. None of the patients had more than 20% of CHD risk equivalent for 10 years. All the females had less than 10% risk equivalent for CHD whereas 11% of male patients had the similar risk. There was a higher number (56%) of male patients having 10-20% of the 10 year CHD risk equivalent.

Metabolic syndrome:

More number of men (88%) had metabolic syndrome than women (80%) (Table 6). A closer examination of the data allowed inferring that female patients could be distributed amongst various groups with 36% having BP, FBS and TG above the cut-off values. 20% of the patients had BP, FBS, TG and HDL contributing towards metabolic syndrome and other groups had 16% and 8% of the patients as mentioned in the table 6. In case of male patients, only one patient had 4 variables (BP, FBS, TG and HDL) contributing towards metabolic syndrome while all others (84%) fell in the group having BP, FBS and TG above the cut-off values.

Table 6. Number of patients identified with metabolic syndrome according to the ATP-III guidelines

	Number of patients				
No. of variables	4[a]	3[b]	3[c]	3[d]	Total
Women (no./%age)	5 (20%)	9 (36%)	4 (16%)	2 (8%)	20 (80%)
Men (no./%age)	1 (4%)	21 (84%)			22 (88%)

a = BP, FBS, TG, HDL; b = BP, FBS, TG; c = FBS, TG, HDL; d = BP, FBS, HDL; e = the percentage is from total number of patients (25 each)

Discussion :

Present work was the first study of its kind on the T2DM population of majorly rural areas of Sirmaur district of Himachal Pradesh, India. Since there is no literature available and hence various aspects of T2DM and underlying associated health conditions are hence unknown in this population. It is known that T2DM is a complex condition with affected persons showing derangements in various other functions[2]. Diabetes is not a fatal condition if managed appropriately otherwise it can cause serious consequences. It has been observed that various derangements can be studied as predictors for T2DM[4, 5, 13, 17].

In order to obtain a general picture of the studied population demographic, anthropometric and biochemical variables were studied. Significantly higher values clearly indicated the association of the diabetes and these variables. In corroboration with the previous studies, anthropometric variables (WHR and BMI) were the predictors for T2DM as were correlated to fasting blood sugar[4-7]. In long-term diabetes, kidney dysfunction is a common observation[20, 21]. FBS and urea showed strong correlation and highlighted impact on kidney health in enrolled T2DM patients. Dyslipidemia has also been considered as a predictor of T2DM[5, 13-15, 17]. In the present study, no direct correlation was observed in case of lipid variables with either FBS or with poor glycemic control (raised HbA1c) which the authors could not explain. In spite of that, a significant correlation between the anthropometric variables and lipid variables was observed. Thus, though indirectly, dyslipidemia can be considered as predictor for T2DM in the present population with caution under consideration.

It is established now that patients with T2DM have metabolic syndrome. MetS is defined as clustering of risk factors including dyslipidemia, abdominal obesity, hyperglycemia and hypertension. Three criteria are available to identify MetS in the diabetic patients. A recent study conducted in Central Indian population of Madhya Pradesh compared

the three prevalent methods for that – WHO definition of 1999, ATP-III criteria by NCEP of 2001 and the International Diabetes Federation (IDF) criteria defined in 2005[22]. Although, IDF criteria were more suited for Asian population, ATP-III guidelines were used in the present work as it gives all the underlying variables equal merit. Besides, it was preferred by Yadav *et al.*[22] for the Indian population as in their analysis, both ATP-III and IDF criteria were in agreement. Another study from Gujarat also analyzed their data based on ATP-III guidelines[23]. Based on these ATP-III guidelines, majority of the population (≥80%) under study had metabolic syndrome. These findings are in consonance with previous studies of T2DM populations of West and Central India[22, 23]. An interesting finding of the present work is that although less number of women showed MetS, wide and varied number of factors contributed. Almost all the men showed same variables as contributing factors thereby, showing uniformity in the disease pattern. It could not be established in the present work if this observation is significant or not, it can still be investigated further with a larger population. As an outcome of the present work, it can be proposed that more number of variables need to be monitored in case of female patients whereas limited variables will be sufficient in case of male patients. The ATP-III guidelines also present with steps for the management of metabolic syndrome. Therapeutic lifestyle changes are suggested for initial three months and then followed by drug treatment if the lipid and non-lipid risk factors persist.

ATP III guidelines consider diabetes as CHD risk equivalent. Also, it warrants a CHD risk equivalent assessment if more than two risk factors (other than LDL) are present. In the present population it was observed that MetS and CHD risk assessment do not overlap strictly. Not all patients with CHD risk had MetS. Also, magnitude of the CHD risk equivalent was also varied amongst the affected groups. The management of CHD risk factors is also indicated in the guidelines. With initial suggestion of therapeutic lifestyle changes for three months followed by specific drug suggestion based on monitoring of the risk factors can be suggested.

Conclusion

WHR and BMI are predictors for T2DM in the study population. Prevalent dyslipidemia was observed with direct correlation to anthropometric variables. All the women had 10% CHD risk equivalent for 10 years. Male population was distributed amongst 10% and 20% CHD risk equivalent. ≥80% of the patients had metabolic syndrome. Higher number of men had MetS as compared to women.

Being the first study of its kind in this backward region of Himachal Pradesh, we now have information that can prove valuable in understanding the pattern of various factors associated with T2DM in the population of this area. It can prove beneficial in paving a path for the systematic management of the disease. A critical shortcoming of the present study is small sample size. However, this work can present itself as a pilot study for designing a study with larger sample size and more number of variables and more robust statistical analysis which may span for a longer period of time and may include the follow-up with constant monitoring of the risk factors after lifestyle changes and drug administration. This will aid in procuring a holistic view of T2DM management in the population of this under developed

district of Himachal Pradesh.

Abbreviations

BMI	Body Mass Index	**MetS**	Metabolic syndrome
CHD	Coronary Heart Disease	**NCEP**	National Cholesterol Education Program
FPG	Fasting Plasma Glucose	**T2DM**	Type 2 Diabetes Mellitus
HbA1c	Hemoglobin A1c	**TG**	Triglycerides
HDL	High Density Lipoproteins	**VLDL**	Very Low Density Lipoproteins
ICMR	Indian Council of Medical Research	**WHO**	World Health Organization
IDF	International Diabetes Federation	**WHR**	Wait Hip Ratio
LDL	Low Density Lipoproteins		

Ethics approval:

It is to certify that the study was performed with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments, further adopted by ICMR.

Consent to participate:

Informed written consent was obtained from the participants included in the study.

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