Original Article

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Comparative Study of the Pattern of Dyslipidaemia among Urban and Rural Type 2 Diabetes Mellitus Population Attending a Tertiary Care Hospital in Eastern Odisha, India

Internal Medicine Section

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ABSTRACT

Introduction: Patients with type 2 diabetes mellitus have increased incidence of obesity and are prone to dyslipidaemia which in turn is the key ingredient of Cardiovascular Disease (CVD). The lifestyle, environment and eating habits significantly vary in urban industrialised areas compared to rural countryside in the same ethnic group.

Aim: To compare the pattern of dyslipidaemia among urban and rural type 2 diabetes mellitus population attending a diabetes follow-up clinic in a tertiary care hospital in eastern Odisha.

Materials and Methods: The cross-sectional study included patients who attended the diabetes follow-up clinic from July 2017 to December 2017 and included adults (≥18 years) suffering from type 2 diabetes. Type 2 diabetics, 300 each from the urban and rural countryside were included in the study. Sociodemographic characteristics, medical history and laboratory investigations like fasting and Postprandial Blood Sugar (PPBS), lipid parameters and HbA1c were recorded. Anthropometric measurements like height, weight, waist circumference and blood pressure were measured. The laboratory values were calculated as mean±standard deviation and correlation analysis with the Pearson coefficient. Z-test was used to compare data at 95% confidence level.

Results: Hypertension was detected in 71% of patients in the urban study sample compared to 34.3% in rural. Obesity was prevalent in 34% of patients in the urban study sample compared to 12.3% in rural. Dyslipidaemia was observed in 86.0% of patients in the urban study sample compared to 66.67% in rural. Finally, physical inactivity was identified in 67.7% of patients in the urban study sample compared to 36.67% in rural.

Conclusion: Blood sugar, both fasting and postprandial was significantly higher in the urban study population as compared to rural. The same variation in HbA1c level was also observed. Incidence of obesity along with dyslipidaemia was more pronounced in urban as compared to the rural population. Obesity and lipid profile showed a positive correlation with HbA1c in both but were significantly stronger in the urban study group as compared to the rural. All the CVD risk factors like hypertension, obesity, dyslipidaemia and physical inactivity were statistically higher in the urban study population as compared to rural.

Keywords: Cardiovascular diseases, Glycosylated haemoglobin, Hypertension, Metabolic syndrome, Obesity

INTRODUCTION

Diabetes has been a growing public health concern worldwide, especially in India which has been termed as the diabetes capital of the world by World Health Organization (WHO). The disease has emerged as a global pandemic and poses a major challenge to health. Initially, restricted to the wealthy and developed nations, diabetes is now spreading to each corner of the world. As per recent studies, the number of people living with diabetes is more in developing countries rather than the developed countries. Among the patients affected with diabetes the number appears to be higher in the urban population than in the rural [1]. As per The International Diabetes Federation (IDF), more than 415 million people worldwide suffer from diabetes as of 2015 and is expected to increase to 642 million by the year 2040 [1]. As per the predictions made by various researches, by the year 2025, the maximum prevalence of diabetes would be in India and every 4th diabetic in the world would be an Indian [2]. The socioeconomic burden caused by this disease is extensive due to a wide spectrum of complications that arise in the long run ranging from Peripheral Vascular Disease (PVD), nephropathy, retinopathy and Coronary Artery Disease (CAD).

In patients suffering from diabetes mellitus, dyslipidaemia is one of the major risk factors for CVD. Around 65% of diabetes-related mortality is due to CVDs [3-5]. As per the recent epidemiologic data, both metabolic syndrome and type 2 diabetes carry an increased risk of CVD [6,7]. The major factors responsible for Coronary Heart Diseases (CHD) and the lipid triad i.e., elevated Triglycerides (TG), decreased High Density Lipoproteins (HDL) and elevated Low Density Lipoproteins (LDL) pose a great risk for development of atherosclerosis in patients suffering from type 2 diabetes [8]. The proportion of LDL has been found higher in patients with diabetes, thereby increasing the risk of CVDs [9,10]. HbA1c, used widely as an indicator of the state of glycaemic control, indicates the glycaemic control over preceding 8-12 weeks, the disease progression, response to treatment and complications arising in patients with diabetes.

Indians are more prone to diabetes because of their food habits and are also predisposed genetically most likely through the interaction of susceptible genes [11]. However, the primary cause of the increasing prevalence of obesity, insulin resistance and subsequent development of type 2 diabetes appears to be the recent environmental and behavioural change [12]. India's growing economy has led to the expansion of urbanised zones, change in the pattern of employment along with increased intake of high fat containing fast processed food [13]. The fast foods being consumed are not only high in fat content but also contain trans fats, which largely contribute to obesity and insulin resistance [14]. The consumption of fast processed food is higher in the urban population (32%) compared to rural areas (17%) [15]. As per the recent statistical analysis, the prevalence of diabetes is 10 folds higher in urban areas as compared to rural areas around the country [15]. Accounting the prevalence of CHD, there is a prominent rural-

urban divide in the prevalence of CHD but the extent of the difference is different in various studies [16].

With the above background of information, a comparative study of dyslipidaemia in type 2 diabetes was conducted between distinct groups of patients from urban and rural population attending the diabetic follow-up clinic of KIMS (Kalinga Institute of Medical Sciences), Bhubaneswar.

MATERIALS AND METHODS

Patients and Protocol

This cross-sectional study was performed in the period of July 2017 to December 2017.

Inclusion criteria: Patients who attended the diabetes follow-up clinic of the tertiary care hospital. The population under study included adults (≥18 years) suffering from type 2 diabetes.

Exclusion criteria: Patients with a history of any acute illness, CVDs and pregnant patients.

Population of Bhubaneswar and Cuttack and 300 type 2 diabetes patients from the rural population belonging to Cuttack and Khordha districts. The sample size was calculated as per the prevalence of CVD risk factors, with 95% confidence level and 5% margin of error. A pretested structured format and a checklist for laboratory results were used to collect the data. A unique identification code was assigned to link the format and checklist. The format of data collection was divided into 3 parts. The first part included socio-demographic characteristics. The second part included the medical history of diabetes, hypertension, and history of drug intake for the same. The final part included laboratory parameters including HbA1c and various lipid parameters. Weight of each study subject being minimally dressed was measured in kilograms (Kg) using WHO weighing scale (Health-O-Meter, USA) and recorded in the case format. Similarly, height of each study subject was measured in centimeters (cm) in erect position and with shoes removed using a stadiometer and was recorded in the case format [17]. Blood pressure of each study subject was measured in each arm after a rest of 15 minutes using a mercury sphygmomanometer and recordings were averaged.

Blood samples for Fasting Blood Sugar (FBS) and total lipid profile was collected at the clinic after 10 hours of fasting. COBAS Integra 400 plus analyser (Roche Diagnostics) was used to determine the FBS, High-Density Lipoprotein Cholesterol (HDL-C), TG level, and serum total cholesterol. HbA1c was measured in the D-10 Haemoglobin analyser (Biorad). Freidwald formula was used to calculate the Low Density Lipoprotein Cholesterol (LDL-C) [18,19].

The patient was labeled as hypertensive if Systolic Blood Pressure (SBP) ≥ 140 mmHg or diastolic blood pressure ≥90 mmHg or patient under treatment for physician-diagnosed hypertension. A BMI ≥30 kg/m^2 or waist circumference ≥102 cm for men and ≥88 cm for women was used to define obesity. Dyslipidaemia was defined as the presence of at least 1 of the following: Plasma total cholesterol ≥200 mg/dl, TG level ≥150 mg/dl, high LDL-C (≥130 mg/dl) and low HDL-C (<40 mg/dl in men or <50 mg/dl in women) [4,5].

Ethical approval: "All the Procedures performed in the study are done as per the ethical standards of the institutional committee and the 1964 Helsinki declaration and its later amendments." The study was approved by the Institutional Ethical Committee of KIMS (Kalinga Institute of Medical Sciences), Bhubaneswar, Odisha, India.

Informed consent: Informed consent was obtained from all individual participants included in the study.

STATISTICAL ANALYSIS

The results were subjected to statistical analysis using Statistical Package for the Social Sciences (SPSS) version 20.0. The laboratory values were calculated as mean±standard deviation and correlation analysis with calculation of Pearson correlation coefficient. Z-test was used to compare data at 95% confidence level and p-value of 0.05 was considered statistically significant.

RESULTS

The biochemical parameters of type 2 diabetes patients from urban and rural study sample are shown in [Table/Fig-1]. We found FBS, PPBS and most crucially HbA1c levels were significantly higher in the urban study population compared to rural. Hypercholesterolemia, hypertriglyceridemia, high levels of LDL was comparatively higher again in the urban study sample compared to rural.

Parameters	Normal values	Urban population (n=300) (Mean±SD)	Rural population (n=300) (Mean±SD)	p-value
FBS (mg/dL)	<100 mg/dL	175.22±68.14	162.34±66.89	0.0196
PPBS (mg/dL)	<140 mg/dL	262.14±88.50	247.24±85.22	0.0361
HbA1c (%)	<5.7%	9.38±2.08	8.22±2.05	<0.0001
Total cholestrol (mg/dL)	<200 mg/dL	205.34±65.41	177.60±44.93	<0.0001
Serum.triglyceride (mg/dL)	<150 mg/dL	186.50±72.81	159.28±44.55	<0.0001
HDL (mg/dL)	<40 mg/dL	43.97±16.63	42.72±11.49	0.2846
LDL (mg/dL)	<100 mg/dL	117.24±40.41	107.16±35.42	0.0012
VLDL (mg/dL)	<30 mg/dL	40.46±28.11	28.71±8.14	<0.0001
TC/HDL-C ratio	<3.5 (Male) <3.0 (Female)	5.04±2.07	4.31±1.21	<0.0001
LDL-C/HDL-C ratio	<2.5 (Male) <2.0 (Female)	3.17±5.16	2.91±5.11	0.5354

[Table/Fig-1]: Biochemical parameters of Type 2 Diabetes patients from urban and rural population.
FBS: Fasting blood sugar; PPBS: Postprandial blood sugar; HDL: High density lipoproteins; LDL: Low density lipoproteins: VLDL: Very low density lipoproteins; TC: Total cholesterol; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low density lipoproteins cholesterol; SD: Standard deviation; value less than 0.05- statistically significant

[Table/Fig-2] describes the socio-demographic characteristics of the study population. In both of the study population, the percentage of males was more than females. Ironically, the percentage of type 2 diabetes patients was maximum both in the urban and rural study population with an educational status of graduation and above.

Characteristics	Urban population (n=300)	Rural population (n=300)	p-value (urban vs rural)
Age (years)			
<35	18 (6.0%)	54 (18%)	<0.0001
35-49	111 (37.0%)	112 (37.3%)	0.9394
50-65	163 (54.3%)	131 (43.7%)	0.0095
>65	8 (2.7%)	3 (1.0%)	0.1226
Gender			
Female	108 (36.0%)	116 (38.7%)	0.4946
Male	192 (64.0%)	184 (61.3%)	0.4946
Educational status			
Illiterate	5 (1.7%)	32 (10.6%)	<0.0001
Upto primary level	50 (16.7%)	44 (14.6%)	0.479
Upto middle	46 (15.3%)	51 (17.0%)	0.571
Upto highschool	56 (18.7%)	56 (18.6%)	0.097
Upto intermediate	55 (18.3%)	57 (19.0%)	0.082
Graduate and above	88 (29.3%)	60(20.0%)	0.008
Family Income (Rupee per month)			
<10000	39 (13.0%)	85 (28.3%)	<0.0001
10000-20000	147 (49.0%)	110 (36.6%)	0.0022
>20000	114 (38.0%)	105 (35.0%)	0.445

[Table/Fig-2]: Socio-demographic characteristic of the Type 2 Diabetes patients from urban and rural population.

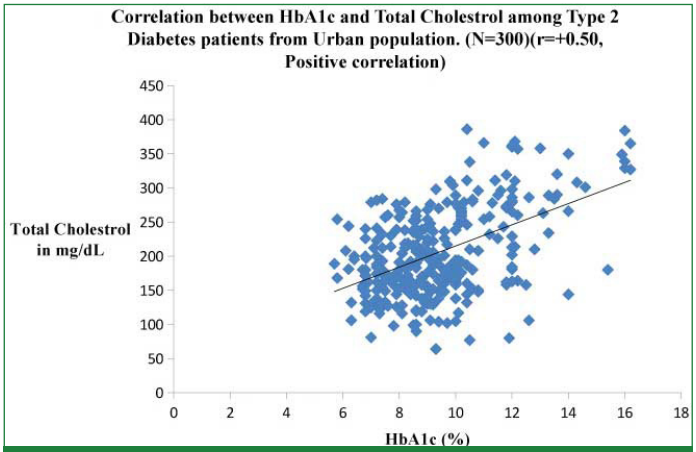
Finally, the percentage of type 2 diabetes patients was found to be non significant elevated in higher income groups in both urban and rural study populations.

The frequency of CVD among the urban and rural study samples is shown in [Table/Fig-3]. Interestingly, all the CVD risk factors like hypertension, obesity, dyslipidaemia and physical inactivity were higher in the urban study population compared to the rural study population.

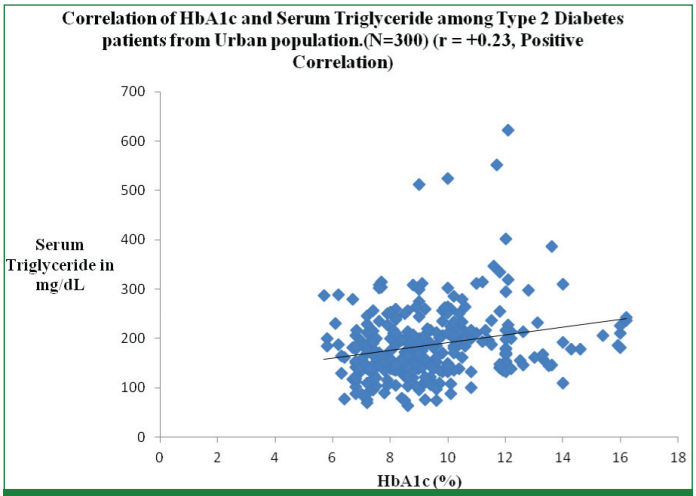
CVD risk factors	Urban population (n=300)	Rural population (n=300)	p-value (Urban vs Rural)
Hypertension	213 (71.0 %)	103 (34.3%)	<0.001
Obesity	102 (34%)	37 (12.3 %)	0.067
Dyslipidaemia	258 (86.0 %)	200 (66.67 %)	0.014
Physical Inactivity	203 (67.7 %)	110 (36.67%)	0.170

[Table/Fig-3]: Prevalence of CVD (Cardiovascular disease) among the Type 2 Diabetes patients from urban and rural population.

[Table/Fig-4-6] shows positive correlations of HbA1c with all three lipid parameters i,e; total cholesterol, serum TG and LDL, in the urban study population with r-value of +0.50, +0.23, +0.40, respectively.

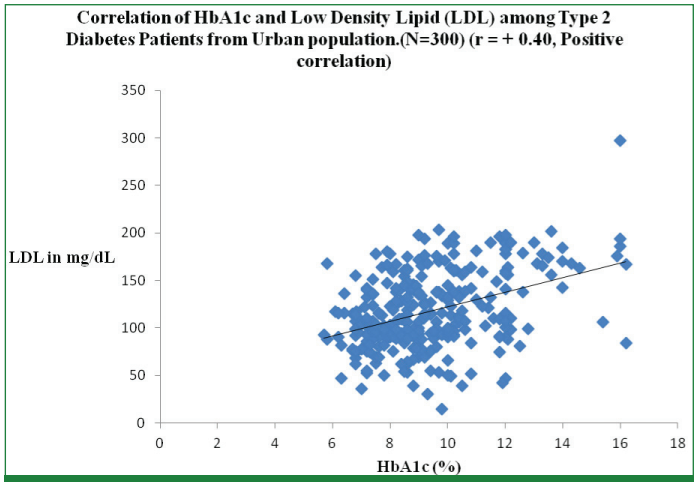


[Table/Fig-4]: Shows correlation between HbA1c and total cholesterol among type 2 diabetes patients from urban population with r value +0.50, positive correlation and p-value <0.00001.

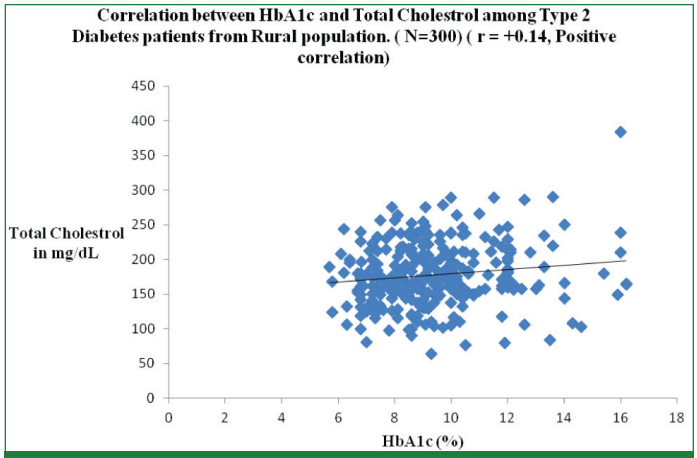


[Table/Fig-5]: Shows correlation between HbA1c and serum triglyceride among type 2 diabetes patients from urban population with r value +0.23, positive correlation and p-value 0.0005.

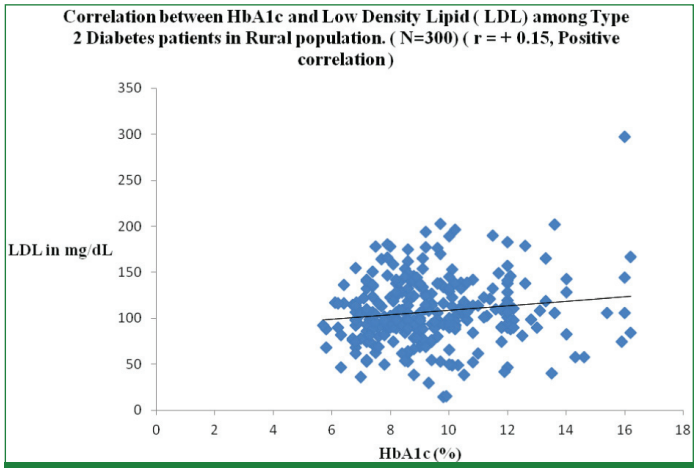
Similarly, [Table/Fig-7-9] demonstrates the positive correlation of HbA1c with the above mentioned lipid parameters in the rural study population with r value of +0.14, +0.15, +0.18 respectively. All three lipid parameters showed a positive correlation with HbA1c in both study population but in the urban study population the correlation was strong as compared to the rural, where it was significantly weak.



[Table/Fig-6]: Shows correlation between HbA1c and Low Density Lipid (LDL) among type 2 diabetes patients from urban population with r value +0.40, positive correlation and p-value <0.0001.



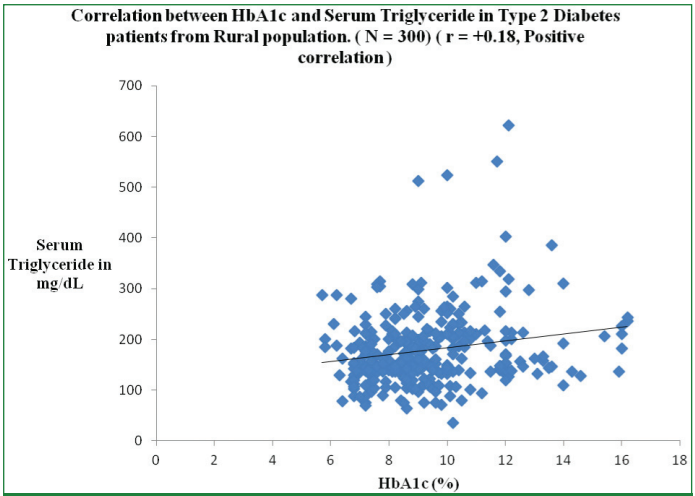
[Table/Fig-7]: Shows correlation between HbA1c and total cholestrol among type 2 diabetes patients from rural population with r value +0.14, positive correlation and p-value 0.015.



[Table/Fig-8]: Shows correlation between HbA1c and Low Density Lipid (LDL) among type 2 diabetes patients from rural population with r value +0.15, positive correlation and p-value 0.009.

DISCUSSION

A 50% of the population with type 2 diabetes have been found to have dyslipidaemia, a known and most important risk factor for CVD [20]. Higher lipid values, hypertension and obesity, usually referred to as metabolic syndrome has been seen in diabetics even before the disease diagnosis [21,22]. These patients are often found to have insulin resistance leading to hyperglycaemia and dyslipidaemia. The metabolic syndrome observed in these patients is the major cause of arterial dysfunction and subsequent life threatening complications [23]. Dyslipidaemia in diabetic patients has been associated with significant co-morbidities characterised by hypertriglyceridemia and reduced serum HDL cholesterol levels. High risk of retention of LDL



[Table/Fig-9]: Shows correlation between HbA1c and serum triglyceride among type 2 diabetes patients from rural population with r value +0.18, positive correlation and p-value 0.0017.

is known to occur around the blood vessels and capillaries; which lead to a high incidence of cardiac diseases. Numerous studies have proven the association LDL cholesterol levels with the risk of developing atherosclerotic cardiovascular events [24].

In this study, FBS, PPBS and most crucially HbA1c levels were significantly higher in the urban study population compared to rural. Hypercholesterolemia, hypertriglyceridemia, high levels of LDL was comparatively higher again in the urban study sample compared to rural [Table/Fig-1].

The metabolism of cholesterol in the human body is balanced by de-novo synthesis, intestinal absorption and excretion through bile and faeces. Intestinal cholesterol absorption and its hepatic transport are mediated by a polytopic transmembrane protein called Niemann-Pick C1 like1 (NPC1L1). In patients with diabetes, there is intestinal overexpression of the protein NPC1L1 [25]. The excretion of the cholesterol from the intestine is mediated by ATP-Binding Cassette (ABC) proteins G5/G8, the expression of which is reduced in diabetic patients. [26]. Both of these abnormal gene expressions in patients suffering from type 2 diabetes are responsible for the high prevalence of hypercholesterolemia.

Apart from other metabolic abnormalities, hypertriglyceridemia is one of the common lipid abnormalities in patients suffering from type 2 diabetes. TG comprises of three molecules of fatty acids and the production of TG depends upon the availability of circulating Free Fatty Acids (FFA) [26,27]. The production of TG occurs in the liver and partly in the intestine [28]. Reaven GM and Greenfield MS, proposed that abnormalities of glucose metabolism cause three distinct syndromes of hypertriglyceridemia [29]. Increased tissue resistance to insulin, compensatory hyperinsulinemia and dyslipidaemia in form of increased VLDL-TG are the primary defects seen in patients with diabetes. Increased hepatic VLDL-TG secretion in response to elevated FFA is seen in conditions with relative insulin deficiency, as it is in type 2 diabetes. However, in type 1 diabetes, the hepatic stimulation is dramatically reduced because of absolute insulin deficiency. This is the reason for reduced VLDL-TG secretion in type 1 diabetes patients despite elevated FFA levels. However, the hypertriglyceridemia observed with type 1 diabetes patients is primarily due to a defect in the process of removal of VLDL-TG [30].

Studies have shown LDL to be one of the best predictors of CVD and the use of statins to lower the LDL levels have been found to dramatically reduce the incidence of CVD in the diabetes population [28]. The outcomes of CVD in diabetic patients is strongly affected by LDL concentrations. The reason behind this is the nature of LDL particles in diabetic patients which are modified to more atherogenic than those of nondiabetic patients. The increased atherogenic property of LDL particles in patients with diabetes is due to their ability to penetrate better into the arterial wall, reduced affinity to the LDL receptors, longer half-life and resistance against oxidative stress [31].

The reason behind increased Very Low Density Lipoprotein (VLDL) pool in patients with diabetes is attributed to their increased production and delayed catabolism [32,33]. It has been shown that in patients with type 2 diabetes, the VLDL production rate correlates with hepatic fat and insulin resistance. The rate of removal of TGs from the circulation is determined by lipoprotein lipase, which is located on vascular endothelium. This lipoprotein lipase is downregulated in conditions where there is insulin deficiency or resistance and this reduction in the enzyme activity contributes to postprandial lipemia [34]. Studies have shown reduction in total cholesterol and TG levels in diabetic patients with improved glycaemic control. This is due to the increased catabolism of LDL by upregulation of receptors and decreased circulating VLDL in the body [35,36].

Limitation(s)

The study included limited subjects and depicted the disease pattern of a particular community rather than the entire nation. More extensive, multicentric trials are required which will bring out the exact burden of the disease in the society.

CONCLUSION(S)

The present study gives some crucial indications about the status of type 2 diabetes patients in rural and urban populations. Though, dyslipidaemia in type 2 diabetes is clinically well established in this study, the degree of severity to be significantly higher in the urban patients compared to rural patients. This fact was further corroborated by the analysis of CVD risk factors in both study groups. Another notable observation was type 2 diabetes is no longer a disease of affluent urban population but has spread in the rural countryside. The increased predominance of fast processed foods higher in fat and trans fat, thereby promoting obesity coupled with physical inactivity resulting in hypertension is a systematic phenomenon in urbanised populations. It not only increases the prevalence of type 2 diabetes but leads to more cases of severe uncontrolled diabetes coupled with dyslipidaemia more prone to CVD. As a take home message, the authors would like to bring out the importance of physical activity and healthy fat free diet in curbing out a disease carrying significant mortality and morbidity from the society.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
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- Manual Googling: May 05, 2020
- iThenticate Software: Jun 27, 2020 (13%)

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- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

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