ORIGINAL ARTICLE

FACTS REVEALED; TOTAL/HIGH DENSITY LIPOPROTEIN CHOLESTEROL VALUES AND THEIR RATIO AMONG MACRO-VASCULAR COMPLICATIONS OF DIABETES

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Objectives: There is key concept that raised mortality among diabetics with stroke, peripheral vascular disease and particularly coronary artery diseases may be owing to dyslipidaemia and its prior detection is needed for timely prevention. Total /HDL cholesterol values and its ratio can be predictive tool among macro-vascular complications of diabetes.

Methodology: A retrospective observational study was conducted in Alamgir Medical Services, airport road Bahawalpur; during a period of 6 months from 30-06-2021 to 30-12-2021.A quantitative data of 100 diabetics with macro-vascular complications were analysed. 52 patients with coronary artery disease (CAD) were identified as group A, 30 subjects had cerebro-vascular accident (CVA) and labelled as group B while 18 patients with peripheral vascular disease (PVD) as group C. Values of lipoproteins and main outcome measure of TC: HDLC ratio were compared between the three groups accordingly.

Results: In patients with CAD, the mean (SD) concentration of total cholesterol (TC) was 220.08(27.9) mg/dl, HDL – C was 34.8 (6.2) mg/dl while TC: HDLC ratio was > 6 and in high risk range (normal ratio should be < 5). Both lipoproteins (TC and HDL and their ratio) were observed within normal range in group B (CVA) as mean SD 180.68(23.4) mg/dl and 35.09(6.9) mg/dl respectively, and in group C (PVD) as 160.20(19) mg/dl and 40.6(5.4) mg/dl respectively.

Conclusion: Diabetics having CAD have raised TC: HDL C ratio and there is advantage to use this ratio for predicting CAD risk.

Keywords: TC: HDL ratio, macro-vascular complications, diabetes

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INTRODUCTION

The demographic survey has estimated that approximately 430 million people are affected with diabetes; 79% of them are in 3rd World countries.[1]

Type 2 Diabetes (T2DM) and related cardiovascular disasters are major public health challenges worldwide.[2] Generally, the drastic consequences of diabetes are characterized by macro-vascular complications such as coronary artery disease (CAD), peripheral arterial disease (PVD), and stroke; >60% of diabetic population is victim of atherosclerotic cardiovascular diseases (ASCVD).[3,4] The diabetics have high prevalence of dyslipidemia resulting more likely hood of ASCVD and conferring independent risks. These individuals harbor cluster of abnormalities that accelerate atherosclerosis: elevated triglycerides and cholesterol; low HDL and abdominal obesity, resulting in increased cardiovascular mortality.[1] Similarly, the prevalence of peripheral vascular disease (PVD) is elevated and incidence of gangrene of foot is 30 times that in age matched control.[5]

The longitudinal studies reveal that among these complications, coronary heart disease (CHD) is due to a distinct diabetic dyslipidemia that is a "biological time bomb". Explicitly the danger of developing CAD is 2-3 time higher in diabetics and also generally they are twice more likely to face cerebrovascular accident (CVA) than people without diabetes, so treating the diabetic dyslipidemia has a beneficial effect.[6,7] Probably it needs mass awareness for prevention and to combat these complications of population at large may be fruitful if endeavor; no cross-no crown. International recommendations are set forth that all diabetic with cardiovascular disease should have measurements of total cholesterol (TC), Triglycerides (TG) and HDL cholesterol (HDL-C) values annually.

In spite of comprehensive research about lipoprotein risk factors for cardiovascular diseases (CAD and CVA), it is yet difficult to define the independent contribution of lipoproteins to atherogenesis. The ACC and AHA do not make LDL the mainstay of their guideline. Millions of people all over the world have CAD and the literature showed that LDL-cholesterol

was not able to identify such patients.[8] The triglycerides are widely accepted to have less consistent effect upon CV events. Emerging trials have bestowed an impression that raised total cholesterol (TC) has identifiable risk and positively associated with CVD mortality,[9,10] it should be "the lower, the better".

Among various lipoprotein measurements, inverse associations between HDL-C and CV diseases have also been observed. Elevated levels of HDL-C are linked with a reduced risk for CV mortality while its decrease level may be an independently increased risk for heart diseases.[10]

Keeping in view the afore mentioned facts about TC and HDL-C, the land mark trials have tested the hypothesis that the TC to HDL-C ratio (TC/HDL) can been widely used as yard stick to predict the risk of CVD among type 2 diabetics.[11] Higher ratios mean a higher risk of heart disease. For this reason, the 2016 USPSTF guidelines recommend that in presence of cardiovascular risk factors particularly diabetes, lipoproteins measurement should commence at age 20 years.[12]

Evidence based research suggests that diabetic people in lower middle-class countries of Asia encounter coronary events at younger age, compared with their Western counterparts.[13] The determinants like housing, food and economy may broadly affect community.

Developing countries have enormous ice berg size health needs and face the highest known rate of CVD. Particularly it is due to poor socioeconomic status, low education and lack of timely preventive treatment. So our paper was focused to assess the hypothesis of correlating lipoproteins values along with TC/HDL ratio among macro-vascular complications of diabetic people and to compare with the value already known internationally by ADA and NCEP.

METHODOLOGY

This retrospective and observational research was designed by reanalyzing quantitative data of 100 diabetic patients with macro-vascular complications.[14] Study was conducted in Alamgir Medical Services, airport road Bahawalpur, during a period of 6 months from 01-06-2021 to 30-12-2021

Ethical Committee approval: It was formally applied to ethical review committee at DME, Quaid-E-Azam Medical College Bahawalpur for conducting research work and had approval no. "966/DME/QAMC BWP". We set out to have written consent from study participants, giving them the autonomy and beneficial effects as well. Confidentiality of data was maintained and study results were disseminated to all the subjects. Retrospective collection of results was not related to human risks. Demographic data was sorted out by review of the patient's medical record. The variables of questionnaire were gender, marital status, personal history, nutritional status, smoking and family history. Body mass index (BMI) was measured according to formula of weight in Kg divided by the square of height in meters.

Macro-vascular complications were determined by using clinical parameters. Customarily typical EKG changes and elevation of biochemical markers like creatinine kinase /MB fraction were used for identification of angina or myocardial infarction. Cerebrovascular disease (CVA) was defined by physical signs as neurological deficits and confirmed with CAT scan brain. PVD was diagnosed on physical examination when absent foot pulses and either history of amputation or gangrene was there.

The lipoprotein values were presented as normal or high-risk category according to recommendations of National Cholesterol Education Program (NCEP) Adult Treatment Panel.[15] According to their guidelines, dyslipidaemia was defined when the total cholesterol was > 200mg/dl and/or triglycerides> 150 mg/dl, and or HDL < 40/ mg/dl. Ratio of TC/HDL was calculated by dividing total cholesterol by HDL number and cut off value was considered below 5. Some authorities recommend target, 4.0 of TC/HD.

TC, HDL-C, and TGs were measured by taking whole blood from venipuncture and using the enzymatic method Cholesterol LDX analyzer. Data was analyzed by using Statistical Package for Social Sciences [SPSS) at version 17. Frequency and percentage variables were computed and quantitative data was presented as Mean ± SD, comparing the lipid levels among groups of macro-vascular complications.

RESULTS

Cross sectional data of hundred diabetic participants with macro-vascular complications was analyzed. Table No.1 demonstrates the clinical characteristics of participants with reference to normal values. Mean (SD) values of systolic B.P was 140 (23mm/hg), while diastolic was 82 (41.5) mm/Hg respectively. The mean (SD) sugar level was 237(103) mg/dl. Collectively the mean (SD) concentration of TC was 187.66 (23) mg/dl, HDLC was 35.6 (5.6) while the triglycerides were 164 (42.6) mg/dl. Higher body mass index (27.5 ± 4) was recorded collectively among participants. "Good things come who wait, bad things for those who weight."

Table 2 display the frequency of macro-vascular complications with lipid profile. It is evident that 52% of patients were victim of coronary artery disease (CAD) followed by 30% cases of CVA and PVD, 18%.

Table 1: Clinical and demographic parameters of subjects

Variables	Reference values	Values
Systolic blood pressure	l35/85	140 ± 23
Diastolic blood pressure	80.21±13.38	82 ± 41.5
Blood glucose random (mg/dl)	200	237± 103
Body mass index	<25	27 .5 ± 4
Triglyceride (mg/dl)	150	164 ± 42.6
Total cholesterol (mg/dl)	200	187.66 ± 23
High-density lipoprotein (mg/dl)	40	35.6 ± 5.6

Table 2. Macro-vascular complications and the comparison with characteristic lipid Profile

	CAD	CVA	PVD
Frequency (N)	52	30	l8
Total Cholesterol (mg/dl)	220.08 ± 27.l	180 ± 23.4	160.20 ± 19
Triglycerides (mg/dl)	170.5 ± 38.4	145.9 1 ± 50.70	170.2 ± 40.49
HDL-C (mg/dl)	34.85 ± 6.27	35.09 ± 6.78	40.6 ± 5.43
TC:HDL-C ratio	6.47	5.1	4 .0

CAD=coronary artery diseases, CVA= Cerebrovascular accident, PVD= Peripheral vascular diseases, HDL= High-density lipoprotein, TC= Total Cholesterol

DISCUSSION

Atherosclerotic cardiovascular disease (ASCVD) has been described and recognized as leading cause of mortality among diabetics owing to accelerated atherosclerosis tagged with dyslipidaemia, the purpose should be the primary prevention of cardiovascular complications.

The ratio of total-to-HDL cholesterol (TC/HDL), known as atherogenic or Castelli index, can be used as cost effective ready reckoner to forecast CAD risk. Our study intended to explore this innovative concept particularly among diabetic patients of CAD.

On the basis of comparing our data, it is reasonable time to consider cut off risk level of HDL (40 mg/dl) and TC (200mg/dl), determined by National Cholesterol Education Program (NCEP ATP) and AHA.[3,15] Considering their guidelines, the TC/HDL ratio should be below 5. It is noteworthy that among our patients of CAD, the said ratio was 6, while the mean HDL-C (34.8 mg/dl) and TC (200 mg/dl) were all-in high-risk range. This ratio was normal in our patients of CVA (5.1) and PVD (4.0), so our further discussion was focused for comparing this ratio among CAD patients owing to fact that diabetes is considered as a CAD risk-equivalent.

Considering raised TC/HDL ratio in our patients of CAD, we compared matching results of the landmark population based and long follow up WHILA trial. Their TC/HDL ratio was categorized into five levels and there was strong association of CAD with higher predictive value at raised 5th quintile (ratio of 5.6).[16] Hazard ratio (HR) was presented and the highest HR in quintile 5 was 2.30 (95% CI: 1.70–3.11) for TC/HDL-C and 1.67 (95% CI: 1.25–2.24) for non-HDL-C.

Similar findings were obtained from a longitudinal study of Swedish National Diabetes Registry. It showed that base line TC (mmol/L) was 5.06 ± 0.99 (192 ± 37 mg/dl) and HDL-C (mmol/L) was 1.31 ± 0.41(49 ± 15 mg/dl) among patients with CAD with total to HDL-C ratio of 4.16 (3.3–4.9).Well craftily patients were followed until faced the first CHD event and simultaneously total to HDL-C ratio was measured regularly. The paramount observation was that rate of CAD continued to increase with increase in said ratio expressing its predictive performance. LDL cholesterol turned out to be non-predictor of CAD risk in type 2 diabetes.[17]

Our ratio of TC/HDL (6.4)[5] was found as a superior marker to be associated with CAD among diabetic patients. Comparing local studies, Shabana and Shahid has shown nearly same findings to ours. Among their patients of CAD and obesity, 49.5% had TC more than normal cut off (> 200 mg/dl) and 64% had HDL values in moderate CHD risk group (< 50 mg/dl).Among diabetic males, TC/HDL ratio was 5.22 and proved to be sensitive predictor of cardiovascular disease risk.[18] They also narrated that this ratio above 5 is considered atherogenic in USA.

In an Indian research it was also concluded that TC/HDL ratio was specific and accurate index for assessing coronary artery disease than considering only TC, TG, HDL, and LDL levels alone. The TC/HDL ratio for their diabetic subjects with CAD was 6.3 and it was much reasonably higher as compared to non-diabetics.[19]

The researchers in a mega trial elaborated useful findings. Their main study outcomes were CVD (re)hospitalization after 90 days. There was significant identical increase in CV events with each 1 unit

increase of TC/HDL ratio above threshold value (2.8) among two groups. The lowest risks of hospitalization due to CVD was found for ratio of TC/HDL at 2.8 (95% CI: 2.6–3.0) in all groups. This was lower with said ratio in the 2.8–4.0 range.[20]

The majority of prior research had shown affirmative judgment while a few had questionable results as well. Iqbal and coworkers concluded that diabetes appeared to express no distinctive impact on levels of lipoproteins among cardiac patients. Among their participants, TC was 186±51 and HDL was 34.2±9.8 while its ratio was 5 (borderline). They suggested that this poor association observed could have been due to lack of characteristic data concerning smoking by the patients.[21] Another possible explanation is relation of ethnic groups with disease progression and effect of socio-economic factors on lipoprotein values and complications.

Contrary results were also obtained by Al-Khawlani A and Atef ZA et al. The TC (mg/dl) was 184.7 and HDL-C (mg/dl) 46.6 while their ratio was 4. They reported low proportionate cases of coronary disease in their research. In fact, their participants were slightly younger and the prevalence of overweight was also considerably lower.[22]

For purpose of correlating ratio of TC/HDL to CAD events, it is high time to discuss Atherosclerosis Risk in Communities (ARIC) study as they had valuable findings. Their enrolled 14,403 participants did not have any cardio-vascular disease at baseline. 2634 cases, with TC/HDL-cholesterol more than the median value of 4.2., suffered atherosclerotic cardiovascular disease events over a median follow-up of 24.2 years. Distinctively it was noted that TC/HDL-cholesterol ratio had unique importance as clinically significant discordance existed between this ratio from the standard clinical data and lipid profile (non-HDL-C and LDL-C). The researchers concluded that this discordance may help atherosclerotic cardiovascular disease risk management, particularly in individuals with diabetes.[23]

Most of the above reported studies have captivated the substantial number of evidence and had ascertained the link of raised TC/HDL ratio to CAD among diabetics.

There were certain limitations in our study. We accept that it was single centered with small sample size and it did not included duration of diabetes along with its treatment. Also risk factors like smoking and sedentary life were not considered due to paucity in the original data.

CONCLUSION

Hypercholesterolemia, low HDL-C and elevated TC to HDL ratio is particularly indicative of coronary events among diabetics.

Health care providers must opt vibrant program for evaluation and prevention of CHD among diabetic along with advice to optimize lifestyle and develop a goal with motivation for population at large to help prevent complications because; “Service to ailing community is rent you pay for your room in heaven".

AUTHORS' CONTRIBUTION:

MAA and IA: Concept and design, data acquisition, interpretation, drafting, final approval, and agree to be accountable for all aspects of the work. MAK and MK: Data acquisition, interpretation, drafting, final approval and agree to be accountable for all aspects of the work.

Conflict of interest: Authors declared no conflict of interest.

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