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Research Article

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Association of Apolipoprotein B /Apolipoprotein A-I Ratio with Cardio Metabolic Risk Biomarkers in Type 2 Diabetes Mellitus

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Abstract

Background: *Individuals diagnosed with Type 2 Diabetes Mellitus and metabolic syndrome are at a heightened risk for cardiovascular disease. Apolipoprotein B (Apo B) is a reliable measure for assessing atherogenic particles, while Apolipoprotein A-I (ApoA-I) plays a key role in antiatherogenic high-density lipoproteins. Timely identification and evaluation of cardio metabolic risk factors can decrease the likelihood of developing CVD.*

Objectives: *This study aimed to evaluate the association of Apo B/Apo A-I ratio with cardiometabolic risk biomarkers in T2DM.*

Materials and Methods: *This cross-sectional study conducted at Tribhuvan University Teaching Hospital and involved 120 individuals diagnosed with Type 2 Diabetes Mellitus who visited the Medicine Outpatient Department, as well as 120 apparently healthy controls. Clinical and anthropometric characteristics were documented using a clinical proforma, and fasting blood samples were collected for the estimation of plasma glucose, Apolipoprotein B (ApoB), Apolipoprotein A-I (ApoA-I), traditional lipid profile analysis, and calculation of the Apolipoprotein B/Apolipoprotein A-I ratio.*

Results: *The mean values of cardiometabolic risk biomarkers and Apo B/Apo A-I ratio in patients with T2DM were significantly higher, whereas HDL-C was significantly lower than that of a control group ($p \leq 0.001$). The Apo B/Apo A-I ratio was strongly positively correlated with LDL-C, TC, Non-HDL-C, and Apo B ($r=0.68$-0.89, $p<0.001$) and modestly positively correlated with BMI, WC, TG, and VLDL-C ($r=0.55$-0.67, $p<0.001$). Additionally, there was a weak but significant positive correlation ($r=0.18$-0.35, $p<0.05$) with weight, systolic blood pressure, and fasting blood glucose. On the other hand, the Apo B/Apo A-I ratio showed a negative correlation with HDL-C and Apo A-I ($r = -0.58$, $p<0.001$).*

Conclusion: *The present study demonstrated that an elevated Apo B/Apo A-I ratio constituted a good association with several cardiometabolic biomarkers and supports that the Apo B/Apo A-I ratio as a potentially useful risk marker for predicting future cardiovascular disease in patients with type 2 diabetes mellitus.*

Keywords: Type2 Diabetes Mellitus, Metabolic Syndrome, Apo B/Apo A-I Ratio, Cardiometabolic Risk Factor

1. Introduction

Type 2 Diabetes Mellitus (T2DM), the most prevalent category, caused by a combination of resistance to insulin action and inadequate compensatory insulin secretion. In Nepal, the estimated pooled prevalence of T2DM was 8.4% in 2015, highlighting the significant burden of this disease in the country [1]. The number of deaths accounted by Diabetes Mellitus were 1270 males, 1080 females in age group 30-69 years, 1370 males, and 1430 females in the age group above 70 yrs [2]. There was 451 million (age 18-99 years) people suffering from diabetes worldwide and expected to increase to 693 million by 2045 [3]. Individuals with T2DM have a twofold increased risk for cardiovascular disease (CVD), which includes myocardial infarction, stroke, and peripheral vascular disease. The principal reasons for death in T2DM patients are CVD. Nearly 80% of the mortality in T2DM is because of CVD [4]. The cluster of cardio vascular (CV)/ metabolic syndrome (MetS) is a major factor responsible for increased CV risk in T2DM [5,6].

Cardiometabolic risk factors includes abdominal obesity, impaired fasting glucose level, hypertension and blood lipid disturbances like low levels of HDL, high fasting and postprandial levels of triglyceride -rich lipoproteins, and elevated levels of small dense LDL particles. All these cluster of cardiometabolic risk factors indicates the MetS. Cardiometabolic risk factor increases the threat of cardiovascular disease occurrence and mortality. Apolipoproteins, a protein component of lipoproteins, are expressed mainly in the liver, partly in the intestine and other tissue.7 Apolipoprotein in the lipoprotein are carriers of hydrophobic molecules like triglycerides and cholesterol esters in the plasma aqueous medium, ligands to the specific receptors on the cell surface of target organ and as coenzymes [7-9]. Apolipoprotein B (Apo B) is an essential structural component of very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), and low-density lipoproteins (LDL). Each of these lipoproteins have Apo B apolipoprotein such that the measurement of Apo B level in plasma will represent the total atherogenic particles [10].

Apolipoprotein A-I (Apo A-I) is the major apolipoprotein associated with high density lipoprotein (HDL). Apo A-I is the main initiator and driver of reverse cholesterol transport. Apo A-I is also responsible for anti-oxidant and anti-inflammatory effects of the HDL. Thus Apo A-I exhibits several anti-atherogenic effects [11]. Therefore, Apo B/Apo A-I ratio reflects the cholesterol balance of the potentially atherogenic and anti-atherogenic lipoprotein particles. Subsequently, its high value would indicate an increased trend to cholesterol deposition, endothelial dysfunction and consequently, higher risk of atherogenesis [12,13]. Several researchers have published their research regarding the benefit of Apo B/Apo A-I ratio in ruling out CVD risk; however, in Nepal the study on Apo B/Apo A-I ratio in patient with T2DM has not been reported till date. Therefore, this study is designed with the aim of investigating the association of Apo B/Apo A-I ratio with cardiometabolic risk variables in T2DM. Apo B/Apo A-I ratio can be a better marker for prediction of cardiovascular risk. As the principal cause of death in T2DM patients is CVD, knowing the Apo B/Apo A-I ratio we can reduce the cardiovascular risk.

2. Materials and Methods

The cross-sectional study was conducted at the Department of Biochemistry in Tribhuvan University Teaching Hospital, Kathmandu. From July to December 2021, 120 individuals diagnosed with type 2 diabetes mellitus visiting the Medicine OPD and 120 apparently healthy controls were included in the study after obtaining approval from the Institutional Review Committee (IRC). All study participants were classified according to the NCEP ATP III criteria of Metabolic Syndrome. The control group consisted of individuals without diabetes mellitus, who had no general health complaints, were not taking any medication, and provided written consent.

2.1. Anthropometry Measurements

Standardized stadiometer and scale were employed for measuring the height and weight respectively. The circumference midpoint between the lowest rib and the iliac crest was detailed as WC. Measurements were carried out with a standardized tape measure, and were rounded off to the nearest centimeter (cm). Blood pressure (BP) was measured by the Korotkov method at rest in a sitting position with a membrane sphygmomanometer as per ESC [14].

2.2. Laboratory Analysis

Fasting blood was sampled, after an overnight fast (8-12 hours) and serum samples were separated for analysis. Lipid profiles and fasting glucose were measured using fully automatic biochemistry analyzers (BT 1500 chemistry analyzer). The measurement of Apo A-I and Apo B was done using the immunoturbidimetric method (Agappe Diagnostics). HBA1C was analyzed in EDTA samples using the Hb-vario HPLC analyzer. All laboratory analyses were conducted following standard operating procedures of the laboratory.

2.3. Calculation

Body mass index (BMI) was represented as the body weight (kg) divided by height squared (m2). The Apo B/Apo A-I ratio was calculated after measuring the Apolipoprotein B and Apolipoprotein A-I.

2.4. Statistical Analysis

Statistical analyses were done by SPSS 20.0version (Statistical Package for Social Science for windows version). Results are presented, as means {±standard deviation (SD) .The significance of differences between means was assessed using Student's t test for data sets. Relationships between quantitative variables were analyzed using Spearman's correlation coefficient. Results were considered as statistically significant or non-significant (NS) for $p < 0.05$ or $p > 0.05$, respectively.

3. Results

3.1. Demographic Distribution of Study Population

In this study 120 T2DM patient with mean age of 54.83 ± 9.578 years as cases and 120 apparently healthy participants with mean age of 54.63 ± 9.44 years as control were recruited. Among them, the numbers of male and female were 129 and 111 respectively Table 1. Most of T2DM patients and controls were from 46-55 years of age group. Similarly, the least number

of cases and controls belong to age group of 35-45 years and of 66-75 years, respectively in Figure 1.

Gender	Cases	Controls
Male	64(53.3%)	65(54.2%)
Female	56(46.7%)	55(45.8%)
Total	120(100%)	120(100%)

Table 1: Demographic Distribution of Subjects

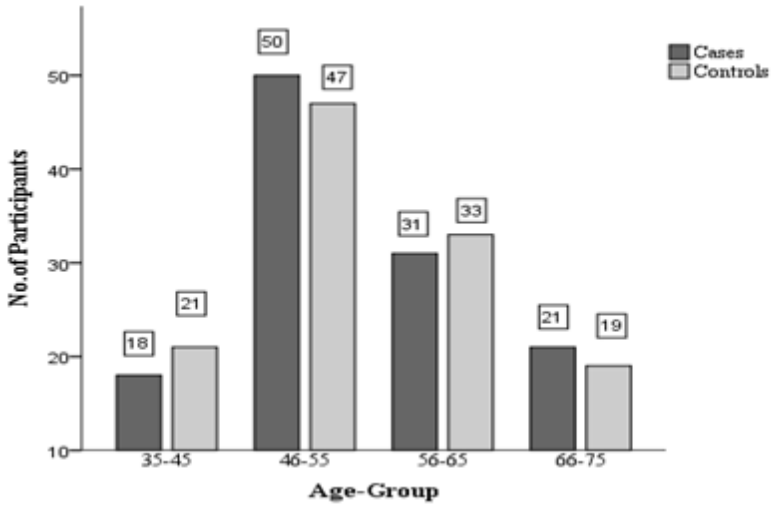

Figure 1: Age Wise Distribution of Cases and Controls

3.2. Anthropometric and Biochemical Characteristic of T2DM and Controls

While comparing the anthropometric and biochemical data between T2DM patients and controls, the mean values of Weight, BMI, WC, SBP, DBP, FBG, HbA1C, TC, TG, LDL-C, VLDL-C, Non HDL-C, Apo B, Apo B/Apo A-I ratio were found to be significantly elevated in T2DM, but that of Apo A-I and HDL-C were higher in healthy controls. The mean value of HDL-C is statistically significant between cases and controls. The mean values of various Variables (with S.D), cases and controls, along with their corresponding p values are shown in Table 2.

Variables	Cases (Mean ± S.D) N=120	Controls (Mean ± S.D) N=120	p value
Age(yrs)	54.83 ± 9.578	54.63 ± 9.44	0.874
Height (cm)	155.50 ± 10.06	155.8917 ± 9.94	0.986
Weight (kg)	61.96 ± 10.96	57.59 ± 8.587	0.010
BMI (kg/m2)	25.43 ± 2.93	23.59 ± 1.70	<0.001
WC (cm)	94.14 ± 9.41	84.15 ± 4.28	<0.001
SBP (mmHg)	127.37 ± 8.71	120.58 ± 5.91	<0.001
DBP (mmHg)	86.45 ± 7.31	79.87 ± 4.46	<0.001
FBG (mg/dL)	151.28 ± 58.14	93.45 ± 12.62	<0.001
HbA1C (%)	7.88 ± 1.51	5.45 ± 0.63	<0.001
TC (mg/dL)	183.17 ± 39.58	148.15 ± 17.30	<0.001
TG (mg/dL)	167.36 ± 76.33	113.35 ± 40.70	<0.001
HDL-C (mg/dL)	36.78 ± 5.05	41.84 ± 4.21	<0.001
LDL-C (mg/dL)	112.81 ± 36.28	83.88 ± 16.66	<0.001
VLDL-C (mg/dL)	33.45 ± 15.23	22.67 ± 8.14	<0.001
Non HDL-C(mg/dL)	146.39 ± 41.27	106.01 ± 18.60	<0.001
Apo B (mg/dL)	107.50 ± 27.19	81.77 ± 16.13	<0.001

Apo A-I (mg/dL)	104.64 ± 13.28	116.52 ±12.22	0.135
Apo B/Apo A-I	1.04 ± 0.31	0.70 ± 0.15	<0.001

Table 2: Anthropometric and Biochemical Characteristic of Cases and Controls

3.3. Distribution of Study Population by Apo B/Apo A-I Ratio Level

Categorized Apo B /Apo A-I ratio was compared between case and control population. This ratio was found to be elevated in the diabetic population group compared to the age- and sex-matched control group Figure 2. In diabetic patients, 54 (45.0%) had desirable level while 66 (55.0%) had CHD risk level of Apo B/Apo A-I ratio.Whereas in control group,114 (95.0%) had acceptable and 6 (5.0%) had CHD risk levels of ApoB/Apo A-I. The frequencies of participants in different categories are shown in Figure 3.

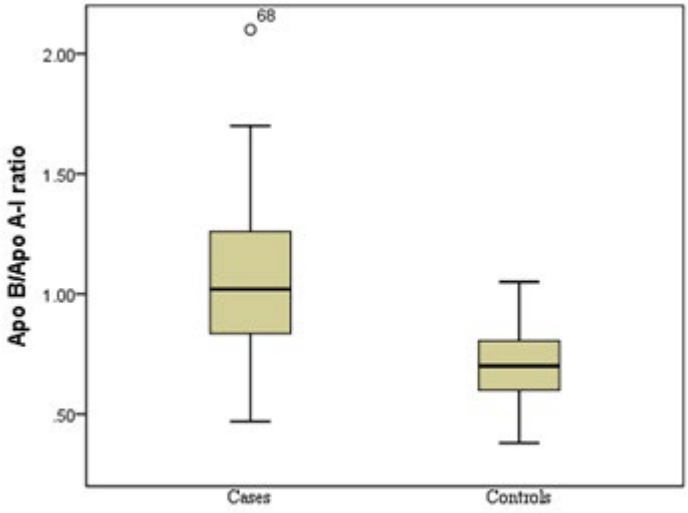

Figure 2: Box Plot Showing Comparison of Apo B/Apo A-I in T2DM Patients and Controls

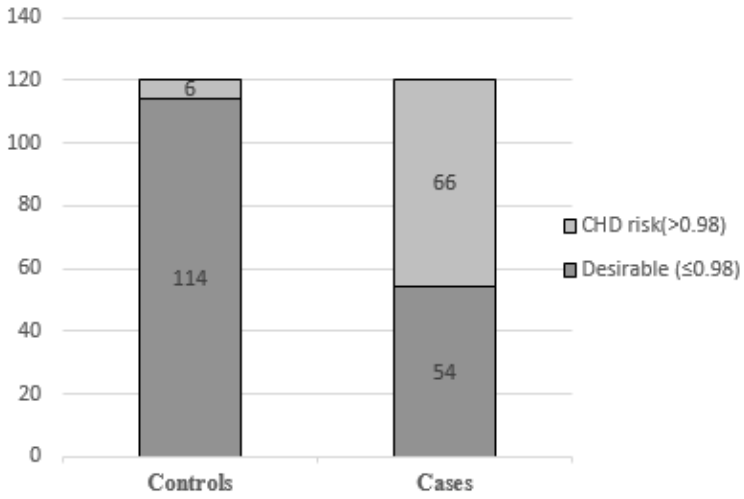

Figure 3: Distribution of Apo B/Apo A-I Ratio Levels in Cases and Controls

3.4. Correlation of Apo B/Apo A-I Ratio with Others Cardiometabolic Risk Biomarkers in T2DM

Apo B/Apo A-I ratio was found to be significantly correlated with Weight, BMI, WC, SBP, FBG, TC, TG, HDL-C, LDL-C, VLDL-C, Non-HDL-C, Apo B, and Apo A-I ratio, whereas the correlation with Height and DBP was statistically insignificant.. There was a strong positive correlation between the Apo B/Apo A-I ratio and LDL-C, TC, Non-HDL-C, and Apo B (r=0.68-0.89, p<0.001). Similarly, modest positive correlation with BMI, WC, TG and VLDL-C (r=0.55-0.67, p<0.001) and a weak, yet significant, correlation (r=0.18-0.35 p<0.05) with weight, systolic blood pressure and FBG. In contrast, the ratio showed negative correlation with HDL-C and Apo A-I (r = -0.58, p<0.001). The correlation coefficients of Apo B/Apo A-I with these parameters, along with the respective p values are shown in Table 3.

	Apo B/Apo A-I Ratio	
Variables	**Correlation Coefficient ®**	**p value**
Height (cm)	-0.039	.670
Weight (kg)	0.357	<0.001
BMI (kg/m^2)	0.614	<0.001
WC (cm)	0.669	<0.001
SBP (mmHg)	0.187	0.040
DBP (mmHg)	0.171	0.062
FBG (mg/dL)	0.294	0.001
TC (mg/dL)	0.861	<0.001
TG (mg/dL)	0.553	<0.001
HDL-C (mg/dL)	-0.557	<0.001
LDL-C (mg/dL)	0.766	<0.001
VLDL-C (mg/dL)	0.553	<0.001
Non HDL-C (mg/dL)	0.894	<0.001
Apo B (mg/dL)	0.898	<0.001
Apo A-I	-0.580	<0.001

Table 3: Correlation of Apo B/Apo A-I with Various Cardiometabolic Risk Biomarkers

3.5. Anthropometric and Biochemical Characteristics of T2DM with and without Metabolic Syndrome

Comparing the anthropometric and biochemical parameters between the diabetic with MetS and without MetS, the mean values of Weight, BMI, WC, FBG, HbA1C, TC, TG,HDL-C, LDL-C, VLDL-C, Non-HDL-C, Apo B, Apo B/Apo A-I ratio were significantly difference. However, the mean values of age, height, SBP, DBP and Apo A-I were statistically insignificant ($p > 0.05$). The mean values of different variables (with S.D), of both MetS and Non- MetS, along with their corresponding p values are shown in Table 4

Variables	MetS (Mean ± S.D) N=93	Non-MetS (Mean ± S.D) N=27	p value
Age(yrs)	54.89 ± 8.93	54.63 ± 11.72	0.078
Height (cm)	155.92 ± 10.25	154.07 ± 9.41	0.352
Weight (kg)	64.56 ±10.60	53.00±6.71	0.010
BMI (kg/m^2)	26.35±2.58	22.26±1.50	0.006
WC (cm)	97.34±7.90	83.11±4.69	0.001
SBP (mmHg)	128.76±8.617	122.77±7.63	0.880
DBP (mmHg)	87.63±7.28	82.22±5.60	0.284
FBG (mg/dL)	163.75±57.63	108.33±35.36	0.001
HbA1C (%)	8.24±1.48	6.64±0.81	<0.001
TC (mg/dL)	194.26±37.55	144.96±15.01	<0.001
TG (mg/dL)	184.52±76.78	108.25±33.52	<0.001
HDL-C (mg/dL)	35.43±4.54	41.44±3.84	0.045
LDL-C (mg/dL)	121.80±35.84	81.85±14.05	<0.001
VLDL-C (mg/dL)	36.88±15.31	21.65±6.70	<0.001
Non HDL-C (mg/dL)	158.83±38.07	103.51±14.36	<0.001
Apo B (mg/dL)	115.22±25.03	80.88±14.78	0.018
Apo A-I (mg/dL)	101.36±11.75	115.92±12.17	0.992
Apo B/Apo A-I	1.1428±0.27	0.7015±0.13	0.002

Table 4: Anthropometric and Biochemical Characteristic of Diabetes with Metabolic Syndrome and without Metabolic Syndrome

3.6. Predictive Significance of Apo B/Apo A-I Ratio for Diabetes Mellitus with Metabolic Syndrome

To study the potential of Apo B/Apo A-I ratio to predict the diabetic metabolic syndrome, ROC curve was plotted. At the cut-off value of Apo B/Apo A-I ratio of 0.86, the sensitivity and specificity were 89.2% and 85.2%, respectively. Increasing the cut-off to 0.90 the sensitivity dropped to 82.8% and the specificity increased to 92.6 %. The ROC Curve showed an area under the curve value of 0.938 (95% CI: 0.897- 0.980, P<0.001) Figure 4.

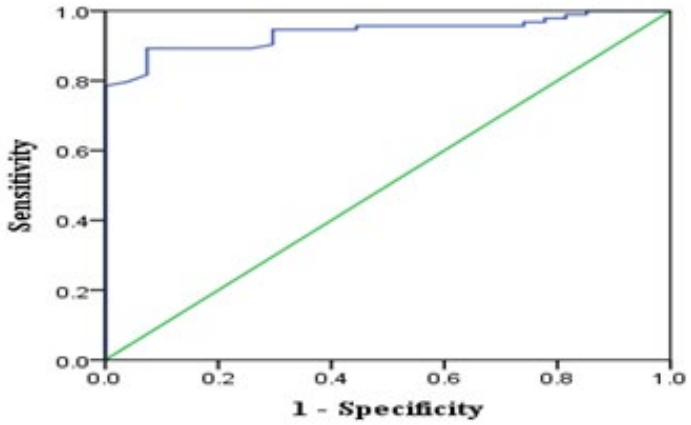

Figure 4: ROC Curve Plot of Apo B/Apo A-I Ratio for Diabetic with Metabolic Syndrome

4. Discussion

Present study was conducted to find the association of Apo B/Apo A-I ratio with various cardiometabolic risk biomarkers like height, weight, BMI, waist circumference systolic and diastolic blood pressure, total cholesterol, triglycerides, HDL-C, LDL-C, VLDL-C, Non-HDL-C, Apo B, Apo A-I in T2DM. Majority of the diabetic patients (68.4%) were aged 46-65 years. This result is similar with the global estimates of diabetes where the majority of diabetic patients in developing countries are between 40 and 60 years [15]. The NCEP ATP-III definition of MetS was used here for describing the diabetic patients with or without metabolic syndrome [16]. Regarding the anthropometric measures, the mean differences between diabetic and healthy controls were significant in the context of BMI, WC, systolic and diastolic blood pressure. However, the significant mean differences were noted for diabetic with metabolic syndrome in BMI ($p = 0.006$) and WC ($p = 0.001$) compared to diabetic without metabolic syndrome. Thus, WC and BMI anthropometric markers need to be rigorously monitored to delay or prevent MetS and consequently the greater risk of CVD.

In addition to blood sugar and HbA1c, lipid profiles (TC, TG, HDL-C, LDL-C, VLDL-C and Non- HDL-C) were significantly deranged in T2DM compared to healthy controls. Our pattern of lipid profile derangement was similar to previous studies done on diabetics, showing increased levels of TC, TG, and LDL-C and decreased levels of HDL-C [17-20]. In this study, Apo B/Apo A-I ratio was elevated in diabetic patients and diabetes with metabolic syndrome, putting this group and subgroup in CHD risk level. Increased Apo B/Apo A-I ratio level was also significantly increased in diabetic patients, which is in agreement with results of Gao l et al [21]. Jun JE et al. publicized that an increased Apo B/Apo A-I ratio was significantly linked with carotid atherosclerosis in low LDL-C level T2DM patient [22]. Increased Apo B/Apo A-I ratio is associated with increased CVD risk in young people. Several large studies realized that the ApoB/ApoA-I ratio was potently predictive of MI risk. The AMORIS (Apolipoprotein-related Mortality Risk) study showed that ApoA-ApoB, the ApoB/ApoA-I ratio and I were stronger predictors of fatal MI risk than TC or TG [23].

In this study, Apo B/Apo A-I ratio has shown good association with cardiometabolic risk markers, the positive correlation with various variables of the study was observed except for HDL-C and Apo A-I. This study showed that, LDL, TC and TG were positively correlated with Apo- B and Apo- B was negatively correlated with HDL-C are in keeping with Kumar S et al, and Katulanda GW et al and also with non HDL cholesterol like Adaja T et al and Jiang R et al who showed that there was a positive correlation of Apo B between TC, LDL-C, Non HDL-C [24-27]. In contrast to Adaja T et al this study showed the correlation of Apo B with BMI and TG [26].

The combined effect of Apo B and Apo A-I is realized in the Apo B/Apo A-I ratio, which showed a highly significant correlation with cardiometabolic risk biomarkers. Recent studies have used the Apo B/Apo A-I ratio is associated with cardiometabolic risk biomerkers [28]. The findings were consistent with Sahadevan DC et al described a relation between the Apo B/Apo AI ratio and cardiometabolic risk factors in patients with MetS and patients without MetS, and the study reported a higher Apo B/Apo A-I ratio in the MetS subjects than the control subjects [28]. Apo B/Apo A-I ratio was positively associated with various cardiometabolic risk factors including TG, WC, systolic and diastolic blood pressure, and fasting plasma glucose, The number of MetS components may have a relationship with Apo B/Apo A-I ratio [12,29]. To the best our knowledge, our study is the first to demonstrate a significant association of the Apo B/Apo A-I ratio with various cardiometabolic risk biomarkers (Weight, BMI, WC, SBP, FBG, TC, TG, HDL-C, LDL-C, VLDL-C, Non

HDL-C, Apo B, HDL-C and Apo A-I) in T2DM in Nepalese population.

There is substantial evidence from epidemiological studies supporting a high Apo B/Apo A-I ratio as a promising risk marker of future cardiovascular events better than any of the cholesterol indexes [30-33]. Moreover, several earlier cross-sectional studies have demonstrated that the Apo B/Apo A-I ratio was significantly associated with MetS and its components independent of conventional risk factors [12,34-36]. Apo B/Apo A-I ratio is significantly associated with the major aspects of dyslipidemia, as well as insulin resistance, and the metabolic syndrome, making it an supreme marker for increased cardiovascular risk aside from the conventional lipid markers [13].

Schmidt et al, prospective study, comprising 391 adult males who were followed up for 6.6 years, it was perceived that the Apo B/Apo A-I ratio showed an association with atherosclerosis in the femoral artery and increased cardiovascular risk [37]. The three large cohort studies had demonstrated a consistent outcome that both Apo B and Apo A-I were unbiased and equal predictive values, and Apo B/Apo A-I ratio was the strongest and most precise indicator for cardiovascular disease that was superior to the cholesterol ratios [30,38,39]. Therefore, Apo B/Apo A-I ratio demonstrates better ascendency over the cholesterol ratios in terms of predictive ability.

ROC analysis was performed in our study to assess the cut-off diagnostic value of Apo-B/Apo-A-1 ratio for diabetic patients with metabolic syndrome. The optimal cut-off value of Apo-B/Apo-A-1 ratio for diabetic mellitus with metabolic syndrome detection was 0.86 with a sensitivity of 89.2% and a specificity of 85.2%. Adequate cut-off for the prediction of diabetes with MetS is not well established but few studies have determined the appropriate cut-off values of the Apo B/Apo A-I ratio for the detection of MetS in individuals. Pistavos et al suggested a ratio of 0.73 as an optimal cut-off for predicting metabolic syndrome, with a sensitivity of 74% and a specificity of 67% in Greek population [40]. Jung et al. reported the sex-specific optimal Apo B/Apo A-I ratio cut-off values in a Korean population, 0.65 in men and 0.62 in women [36]. Besides, Jing et al. suggested an optimal Apo B/Apo A-I ratio cut-off value of 0.85 in men and 0.80 in women in a Chinese population [35]. Correspondingly, The INTERHEART and AMORIS studies advised that an Apo B/Apo A-I ratio of 0.90 for men and 0.80 for women were indicative of a high CVD risk, and values of less than 0.70 in men and 0.60 in women were considered to indicate low CVD risk if no other risk factors were present [23,41]. These differences of Apo B/Apo A-I ratio cut off could be due to the genetic polymorphisms, geographical variation, ethnicity, diet and difference in sample size. Medical evidence for Apo B/Apo A-I ratio in the prediction of diabetic with metabolic syndrome is insufficient. Thus, additional studies are necessitated to further strengthen the advantage of this parameter.

Apolipoprotein consider as a chief of all for predicting risk of CVD [42]. CVD is the chief cause of mortality and morbidity in diabetic patient and the NCEP III has termed diabetes a coronary heart disease risk correspondent [43,44]. The Apo B/Apo A-I ratios has many benefits that exceed their use compared with normal lipid parameters and their ratios in predicting CVD. As Apo B/Apo A-I ratio reflects the balance of atherogenic and atheroprotective particles as they represent the amount of vehicles to carry cholesterol. So elevated the level, the greater the tendency of cholesterol deposition, and consequently the higher risk of CVD [45]. Another important feature, the concentration of apolipoproteins are not affected by meals and are slightly influenced by biological variables, unlike the ordinary lipid parameters, which fluctuate widely depending on food intake. Therefore, apolipoproteins measure does not require fasting blood samples [23,46-48]. Consistently, in clinical practice, apolipoproteins B and apolipoprotein A-I may be measured directly in plasma using internationally standardized method without noticeable interference with high triglyceride levels [8,46].

4.1. Limitation

- This study was performed using a cross-sectional design and did not control for potential biases from physical activity, diet, drinking and smoking history.
- This study did not assess long-term outcomes with respect to the occurrence of CVD and the levels of lipid parameters.
- The study would not show the relation of Apo B /Apo A-I ratio with different biomarkers of inflammation which are also responsible for the CVD.

5. Conclusion

In conclusion, the present study demonstrated that an elevated Apo B/Apo A-I ratio constituted a good association with cardiometabolic biomarkers and supports that the Apo B/Apo A-I ratio as a promising marker of future cardiovascular disease. WC and BMI anthropometric markers can also be rigorously monitored to delay or prevent MetS and consequently the greater risk of CVD.

Recommendation

Apo B/Apo A-I ratio associated with biomarkers of cardiometabolic risk can be used as potential marker for diagnosis of metabolic syndrome. Metabolic syndrome is major worldwide public health challenge meanwhile it is associated two- to three-fold risk of CVD. As Apo B/Apo A-I ratio reflects the balance of atherogenic and atheroprotective particles, so elevated the level, the greater the tendency of cholesterol deposition, and consequently the higher the risk of CVD. Due to dual function of Apo B/Apo A-I ratio, it is recommended to incorporate in routine test. Methods for determining Apo B and Apo A-I are internationally standardized and automated, analyses are cheap, and more importantly, can be performed on non-fasting samples. Further examination of the association of Apo B/Apo A-I between the number of MetS criteria and pro and inti-inflammatory markers, in a large cohort studies may provide a better assessment for CVD. In addition, a prospective and well-controlled study would be needed to elucidate the associations of Apo B/Apo A-I ratio with diabetes and CVD risk. Similarly, prospective follow-up studies are required to evaluate medical interventions and lipid goal attainment in relation to mortality in diabetes patients with MetS.

Author's Contribution

Hari Sharan Makaju, Vijay Kumar Sharma, Binod Kumar Yadav, Eans Tara Tuladhar and Roshan Bhandari conceived the design of the study.

Hari Sharan Makaju, Aseem Bhattarai, Anant Neupane and Rabina Ramtel performed the acquisition of data.

Hari Sharan Makaju, Binod Kumar Yadav, Vijay Kumar Sharma, Aseem Bhattarai and Eans Tara Tuladhar analyzed and interpreted the data.

Hari Sharan Makaju, Rabina Ramtel, Alisha Sapkota, Anant Neupane, Raju Kumar Dubey and Aapekshya Niraula Drafted the manuscript.

Hari Sharan Makaju, Vijay Kumar Sharma, Mithileshwor Raut, Aseem Bhattarai and Roshan Bhandari performed the critical revision for important intellectual content.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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Approval of the Study

This study has been approved for Master's level thesis by Department of Biochemistry, Institute of Medicine

Ethical Approval

The study has given ethical clearance by the institutional review committee, Institute of Medicine and the letter has been submitted along with the manuscript submission.

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