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Original Article

Relationship among obesity, blood lipids and insulin resistance in Bangladeshi adults

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ABSTRACT

Introduction: Insulin resistance (IR) and abnormal lipid profiles are the risk factors for cardiovascular diseases in obesity. To clarify the relationship of the changes in insulin resistance, body weight and lipid profile, the present study was performed on Bangladeshi adults, total of 1500 individuals at the time of their general health examination in the hospital.

Methods: After exclusion of other endocrine diseases, the remaining 772 patients were classified as IR $\geq$ 2 and IR < 2 based on the homeostatic model assessment-estimated insulin resistance (HOMA-IR) index. The endocrine disease free subjects were further clustered based on age, gender and obesity. The anthropometric and biochemical profiles were statistically analyzed and correlated with IR $\geq$ 2 and IR<2 groups as well as other clusters of the subjects. Apart from some disparities, notable differences were observed in all anthropometric data.

Results: Total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) and serum insulin levels were significantly higher in IR $\geq$ 2 group in comparison with IR<2 group. Obesity and dyslipidemia were associated as prevalent components of IR. Generalized linear model revealed that TC: LDL and TG: HDL had significant effect on IR. Age group II (41–60 years old) subjects had significantly higher lipid profile compared to age group I (20–40 years old) and age group III (61–80 years old).

Conclusions: Results reported herein support the notion that lipoprotein ratios might be the reliable biomarkers to evaluate IR.

1. Introduction

Insulin is a polypeptide hormone that involved in regulation of glucose utilization by acting on different target tissues. Insulin involves a wide variety of cellular actions on signalling pathways by different target cell receptor [1]. When glucose concentration in blood is increased, insulin controls glucose homeostasis by increasing glucose uptake and clearance of glucose with different target tissues. The activation of tyrosine kinase results in autophosphorylation [2]. The adaptor protein insulin receptor substrate 1 (IRS1) is a major substrate of the insulin receptor, associated with signalling pathway and defect in recycling the receptor results in an accelerated receptor degradation and consequent insulin resistance [3].

Insulin resistance is a cluster of related metabolic abnormalities of hyperinsulinemia, glucose intolerance, increased low density lipoprotein, decreased high density lipoprotein, and hypertension [4]. Insulin resistance is a pathophysiological state at which cells fail to respond normally to insulin and a given quantity of insulin produces a less than expected natal effects. It is characterized by decreasing sensitivity of target tissues to the action of insulin by elevated blood glucose concentration and increased hepatic production of atherogenic lipids. According to other views, it is a genetic and molecular ambiguity which involves defective insulin signaling and transport of glucose into cells [5]. Insulin is known to regulate multiple biological functions by association of LDL receptor with insulin receptor and their dissociation by insulin [6].

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Metabolic syndrome is a crucial factor for causing type 2 diabetes mellitus (T2DM) and obesity in South Asians [7]. At approximately 20–25% urban South Asians consistently observed evidence of the metabolic syndrome [8]. It is particularly important to effectively implement and strengthen diagnostic criteria for the prevention of 'epidemic' of obesity and the metabolic syndrome [9].

There is a close relationship between insulin resistance and dyslipidemia. Low density lipoprotein (LDL) particles exist in numerous subclasses which differ in density, size, and lipid content. There are two forms of small LDL, which is strongly related to endothelial metabolism. It also stimulates nitric oxide production and angiogenesis [10]. Insulin resistance, at the level of the fat cell initiating insult, leads to increased intracellular hydrolysis of triglycerides (TGs) and release of fatty acids into the circulation. Due to the molecular or environmental origin for insulin resistance in adipose tissues, the free fatty acid (FFA) uptake by fat cells is decreased or FFA release from fat cells is increased. The absence of fat or the abundance of fat is linked to increase fatty acid instability to the liver and successive increased secretion of very low density lipoprotein (VLDL) [11].

Ethnicity is known to be a potential cause of insulin sensitivity. South Asians have high levels of LDL cholesterol comparable to other population and these LDL particles are more oxidized and circulating lipid peroxidation products are increase in type 2 diabetes mellitus [12]. High level of HDL consistently associated with longevity in diverse populations. Furthermore, low HDL and high LDL which occur more commonly in insulin resistant subjects were shown to predict diabetes in South Asian population. In fact, Indians are in the higher risk of developing T2DM by 2025 [13]. South Asians usually have high percentage of body fat, abdominal obesity, insulin resistance, hyperinsulinaemia and low muscle mass. In particular, abdominal obesity is common in South Asians, which corresponds to increased whole-body insulin resistance, and there is altered endothelial function in this population [14]. However, the awareness is increasing because of lower thresholds of body mass index (BMI) for South Asian adults [15]. One may assume that internationally recommended screening strategies should be adjusted for South Asian [16]. However, very few studies have been done on Bangladeshi subjects to determine the relationship of insulin resistance to obesity and blood lipid profiles, or to determine any biomarker for assessment of insulin resistance. The present study was done to report the relationship among fatness, blood lipid and insulin resistance in Bangladeshi adults aged from 20 to 80 years. This study revealed that obesity and dyslipidemia are the most prevalent components of insulin resistance.

2. Methods

2.1. Population consideration, clustering and sample collection

After getting approval from the Hospital Management, patients of 20–80 years old were contacted to ensure their presence during the study procedure. Histories were collected from 1500 patients, who received an annual health check-up during July 2013 to June 2014. Subjects with endocrine disease (thyroid disorder), significant renal or hepatic disease, coronary artery disease, or cerebrovascular disease and those receiving medications for diabetes mellitus or hyperlipidemia were excluded from the analysis. We could select finally total 772 patients that were subjected to anthropometric measurement and blood samples were collected from these patients for biochemical analysis. The clustering of the subjects considered for the study is shown in Fig. 1. All subjects signed a written consent before being interrogated and physically examined by a trained team. The protocol was approved by the ethical review committees of North East Medical College, Sylhet, Bangladesh.

2.2. Anthropometric analyses

A standardized questionnaire was administered including information on demographic factors, socioeconomic status (education, income), lifestyle (smoking, physical activity, and dietary patterns), medication use, personal and familiar history and risk factors (hypertension, T2DM, dyslipidemia). Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer. Weight was measured to the nearest 0.1 kg with calibrated scales. To calculate the BMI, the body weight (kg) was divided by the height (m^2). The assessment of blood pressure was done applying the auscultatory technique [17]. Obesity was classified according to the criteria of WHO based on the BMI value [18].

2.3. Biochemical analyses

Biochemical variables (including fasting glucose, insulin and lipid profile) were measured by standard methods. Biochemical analyses were done by a clinical chemistry analyzer (Siemens, Germany) using kits supplied by BIO-RAD laboratories, USA. Serum insulin was determined by radioimmunoassay using a commercial kit (BI-INSULIN IRMA; BIO-RAD, Marnes 1a Coquette, France). The ratios of lipid TC/HDL, LDL/HDL & TG/HDL were calculated as described previously [19].

2.4. Insulin sensitivity analyses

Insulin resistance was measured by a homeostatic model assessment (HOMA-IR) index (Fasting plasma glucose [mmol/L] X fasting plasma insulin [μU/mL]/22.5), as described by Matthews and colleagues [20]. Bermdez et al. [21] determined that the optimal cut point for IR for Venezuelan population is 2.00.

3. Statistical analyses

Statistical analyses were performed and the results were expressed as a mean ± standard deviation (SD). *P*-value <0.05 was considered statistically significant. All variables were checked for normality and Pearson's correlation coefficients were used to identify significant association between anthropometric and biochemical parameters. Correlation co-efficient was performed to examine correlation between various parameters. To identify which set of variable best explained the variation, we examined several combinations of these variables in regression models. Predictors for blood insulin and TG were identified by multiple linear regression analysis. The differences between arithmetic means were assessed using *t*-test (when two groups were compared) or one-way analyses of variance (when three groups were compared). Complete data analysis was performed using statistical software R (https://cran.rstudio.com/bin//windows/base/old/3.1.2/).

4. Results

4.1. Anthropometric and biochemical events associate with insulin resistance

During initial stage of our study, we included 1500 individuals. After exclusion of the patients carrying other endocrine disease (thyroid disorder, pancreatic disease), for our assessments, we considered 772 individuals, which carried only the target diseases viz. obesity and DM. These patients were classified as insulin sensitive and insulin resistance; male and female; obese and non-obese subjects. We evaluated the effects of different variables on insulin resistance ($IR \geq 2$) and insulin sensitivity ($IR < 2$) groups. The anthropometric and biochemical variables of insulin sensitivity

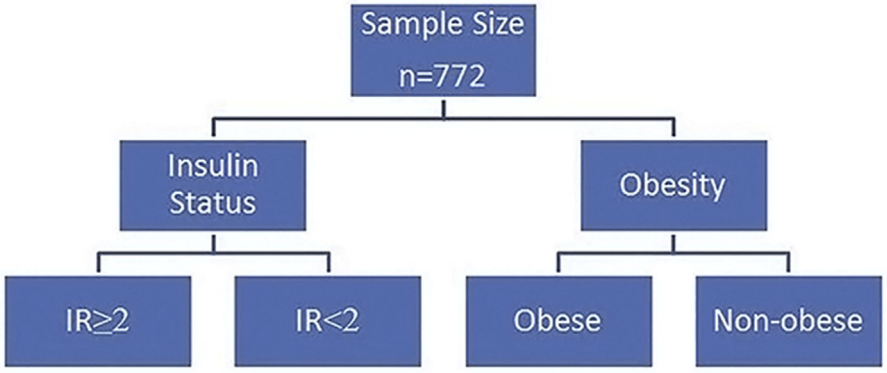

Fig. 1. Clustering of the subjects considered for the study.

and resistance groups were shown in Table 1. Notable differences were found in all anthropometric data. However, there was no remarkable difference in age between insulin sensitivity and insulin resistance groups. Blood pressure was significantly higher in insulin resistance group compared to the insulin sensitive group. Significant differences in age, BMI, systolic and diastolic blood pressure were present in both male and female individuals. Both insulin secretion and sensitivity were significantly reduced in insulin resistance group as compared to the insulin sensitive group. In this study, we used fasting insulin and the HOMA-IR as markers of insulin resistance and risk of future metabolic events. Significant differences in age, BMI, systolic and diastolic blood pressure were present in both male and female individuals. The level of significance in all cases is indicated by p-value<0.05. From all the measured biochemical parameters, we observed a significant difference on TG between obese and non-obese groups. Subjects with a higher BMI were more likely to be obese and insulin resistant. The levels of fasting serum insulin, total cholesterol, low density lipoprotein (LDL) and TG were significantly higher in IR $\geq$ 2 group compared to IR < 2.

4.2. Lipid phenotypes in insulin resistance

Cluster analyses enhances sorting of the subjects, allowing for evaluation according to biochemical and anthropometric variables, eliminating the bias observed in predetermined variables and cut-off points. To study the relative impact of various factors in determining blood lipid levels or insulin sensitivity, multiple logistic regressions were performed. Regression analyses were done for the lipid parameters and lipid ratio with IR in total subjects shown in Table 2. During assessing the effects of lipid status with insulin resistance, we found significant differences on LDL, HDL & TG. However, similar analysis done for the lipid ratio showed only significant effect of TG: HDL. We fitted logistic regression model of diabetic (FBS>7) and non-diabetic (FBS<7) subjects on TC: HDL, LDL: HDL, TG: HDL. The results revealed significant effect on TC: LDL and TG: HDL shown in Table 3.

4.3. Degree of insulin resistance & dyslipidemia in subjects with different age group

To study three age groups with their metabolic health status, patients were divided into three age categories (20–40, 41–60 and 61–80 years). ANOVA was performed to investigate the mean levels of IR for different age groups. A high p-value (0.564) indicated that there was no significant difference in mean IR levels for different age groups (Data not shown). We also performed ANOVA test for mean level of BMI among three age groups of the total population. As we found significant difference (p-value <0.0001) in BMI of three age groups, Tukey's multiple comparison was reported in Table 4. Considerable differences between age group 41–60 years (Group I) to 20–40 years (Group II) and 61–80 years (Group III)

Table 1
Characteristics of subjects categorized by insulin status and obesity.

Variable	Insulin Status				Obesity			
	IR ≥ 2	IR < 2	t-value	p-value	Obese	Non-obese	t-value	p-value
Age	52.60 ± 14.44	54.09 ± 15.51	1.29156	0.197	54.71 ± 14.161	49.36 ± 15.634	−4.4801	0
Height	158.74 ± 6.34	159.34 ± 6.53	1.21853	0.223	158.56 ± 6.112	159.84 ± 6.958	2.42604	0.0157
Weight	62.43 ± 7.11	63.36 ± 7.03	1.73076	0.084	64.98 ± 6.063	57.60 ± 6.597	−14.582	0
BMI	26.04 ± 2.57	26.22 ± 2.56	0.92032	0.357	27.34 ± 1.972	23.25 ± 1.099	−36.624	0
SBP	124.62 ± 12.39	123.30 ± 12.04	−1.43	0.0003	125.07 ± 10.798	122.13 ± 14.963	−2.7038	0.0072
DBP	64.84 ± 8.24	64.41 ± 8.09	−0.6999	0	65.24 ± 7.983	63.43 ± 8.490	−2.7703	0.0059
TC	193.80 ± 57.07	174.66 ± 50.31	−4.7572	0	190.18 ± 55.025	180.60 ± 56.235	−2.1793	0.0298
HDL	34.89 ± 10.10	40.16 ± 10.81	6.52477	0	37.12 ± 10.711	35.75 ± 10.404	−1.6572	0.0982
LDL	122.72 ± 46.64	108.93 ± 43.17	−4.0731	0.000053	118.78 ± 44.576	116.26 ± 48.916	−0.6731	0.5013
TG	214.39 ± 136.36	154.77 ± 97.03	−6.9762	0	200.03 ± 136.845	179.83 ± 100.921	−2.2738	0.0233
Non-HDL	158.90 ± 54.73	134.51 ± 48.88	−6.2762	0	153.06 ± 53.707	144.85 ± 54.234	−1.9278	0.0545
TC:HDL	5.90 ± 2.15	4.60 ± 1.69	−9.1611	0	5.49 ± 2.085	5.36 ± 2.129	−0.7454	0.4564
LDL:HDL	3.71 ± 1.51	2.89 ± 1.39	−7.4935	0	3.42 ± 1.492	3.45 ± 1.587	0.26479	0.7913
TG: HDL	7.14 ± 6.94	4.33 ± 3.58	−7.3821	0	6.32 ± 6.363	5.85 ± 5.631	−1.0142	0.311
FBS	7.45 ± 2.94	5.21 ± 0.84	−15.893	0	6.60 ± 2.318	6.88 ± 3.305	1.17681	0.2401
IR	4.49 ± 2.81	1.53 ± 0.28	−23.378	0	3.46 ± 2.689	3.53 ± 2.687	0.31192	0.7552

BMI= Body mass index; **SBP**= Systolic blood pressure; **DBP** = Diastolic blood pressure.

Table 2
Multiple regression analysis of the lipid status and lipid ratio with the number of insulin resistance in total study subjects.

Parameters	Lipid status				Lipid Ratio			
	Estimate	Std. Error	*Z* value	*P* value	Estimate	Std. Error	Z value	P value
Intercept	2.33886	1.16841	2	0.045*	0.45116	1.11673	0.4	0.6862
Gender	−0.255	0.17086	−1.49	0.136	−0.254	0.16629	−1.53	0.1266
Age	0.00582	0.00584	1	0.32	0.00412	0.00579	0.71	0.4763
BMI	−0.0491	0.03249	−1.51	0.131	−0.0536	0.03241	−1.65	0.0981
Sys	−0.0051	0.00719	−0.71	0.476	−0.0043	0.00704	−0.61	0.5411
HDL	−0.0486	0.00849	−5.73	1.0e-08***	0.20015	0.14276	1.4	0.1609
LDL	0.00932	0.00204	4.57	5.0e-06***	0.14705	0.15207	0.97	0.3336
TG	0.0044	0.00094	4.7	2.6e-06***	0.10035	0.03554	2.82	0.0048**

*Level of significance <0.05.
** Level of significance <0.01.
** * Level of significance <0.001.

Table 3
Generalized linear model for diabetic (FBS>7) and non-diabetic (FBS<7) subjects.

Parameter	Estimate	Std. Error	Z value	p-value
TC:LDL	0.533	0.227	2.35	0.01860*
LDL:HDL	0.591	1.090	0.54	0.58746
TG:HDL	1.763	0.480	3.67	0.00024***

*Level of significance <0.05.
** * Level of significance <0.001.

were observed; however, no significant difference was found between Group II to Group III. Age group related insulin resistance was investigated. The prevalence of insulin resistance significantly varied among the age groups. Changes in age related insulin resistance were shown in Fig. 2. Among the three age groups, Group II subjects had significantly higher insulin resistance. Group II was more significantly raised by metabolic factors than others. To correlate the age group related insulin resistance to dyslipidemia, we investigated lipid profiles in all the three age groups. Data showed that insulin resistant group II subjects had significantly higher lipid profile in comparison with other age groups shown in Fig. 3.

Since insulin sensitivity is influenced and associated with other factors such as excess adiposity and dyslipidemia. In this study, we derived an estimate of insulin sensitivity based on anthropometric and routine biochemical parameters. Our observation by comparing the lipid profile between obese and non-obese is that, in both male and female groups, obese had significantly lower HDL-C and higher TG levels than non-obese. In a spearman correlation analyses, we found that weight and BMI positive correlation with glucose, insulin and HOMA. Significant positive correlations were observed for insulin and HOMA with glucose and TGs and significant negative correlations were observed between HOMA and glucose as well as HOMA and insulin were not unexpected because HOMA values were derived from insulin and glucose concentration.

5. Discussion

This study shows that subjects with insulin resistance are associated with a change in lipid phenotype expression. Recent research identified that a genetic component influences the severity of insulin resistance besides the traditional environmental influences such as BMI. In the present study, we demonstrate that subjects with hyper TG were more insulin resistant. This could be related to the increased BMI frequently reported in hyper TG subjects [22].

Studies reviewed that subjects with dyslipidemia are more insulin resistant, even after-correlation with age, sex and BMI. It has been verified that cut-off values of BMI should be lower for South Asians than the current worldwide value [16]. According to concept of genetic origin, insulin resistant is associated with an increase LDL particle number and triglyceride and reduction in HDL cholesterol in South Asian population. Increased BMI indicated subjects with hypertriglyceridemia and after correction for BMI, subjects with hypertriglyceridemia are more insulin resistance compare to the hypercholesterolemia. This finding suggests that several metabolic pathways proceed toward abnormal lipid parameters. Scientists resume that insulin resistance or obesity do not entirely account for the higher lipid ratio and also not for the increased prevalence of dyslipidemia. Insulin resistance is strongly associated with measures of obesity, such as BMI. Indeed, insulin resistance is linked by factors other than obesity, as defined by elevated BMI. Circulating IL-6 concentrations increased with obesity predicted to develop type T2DM [23]. Further studies should be undertaken to investigate the systematic differences between insulin-resistant individuals with high BMI. Insulin resistance was hypothesized to play a major role in dyslipidemia in T2DM. Studies have shown a link between dyslipidemia is the most prevalent component of metabolic syndrome but exact basis of this link is not clear [24,25]. It was reported that elevated triglycerides, and LDL cholesterol, and low levels of HDL cholesterol were present in obese adults [26]. However, in some studies, similar lipid profiles have been reported in obese and non-obese adults with T2DM, in obese normoglycemic adults, and in non-obese adults with impaired glucose tolerance [23,27].

The present study shows that subjects with obese are more insulin resistant compared with controls. Obesity is a cause of insulin resistance, but is also strongly associated with hypertension, dyslipidemia and glucose intolerance. The people with the highest ratio of triglycerides to HDL had 16 times risk of heart attack those with the lowest ratio of triglycerides to HDL [27]. Since this study also revealed the confirmation of abnormal lipid profile and insulin resistance in the obese adults, which, if not controlled may develop a cardiovascular disease, T2DM and other disorders in later life [28]. Hence it confirms the hypothesis that overweight and obese adults have higher fasting plasma glucose, fasting insulin level and abnormal lipid profile relative to their leaner person. In summary, the routine biochemical analyses performed to date have been unable to provide explanation for the insulin status observed in insulin resistance subjects [29].

Table 4
Tukey's multiple comparison of mean level of BMI with different age groups.

Age Group	Difference	Lower	Upper	p-value
(41–60) & (20–40)	0.8687635	0.3348111	1.4027158	0.0004223
(61–80) & (20–40)	1.0100284	0.4190067	1.6010501	0.0001943
(61–80) & (41–60)	0.1412650	−0.3731842	0.6557141	0.7953485

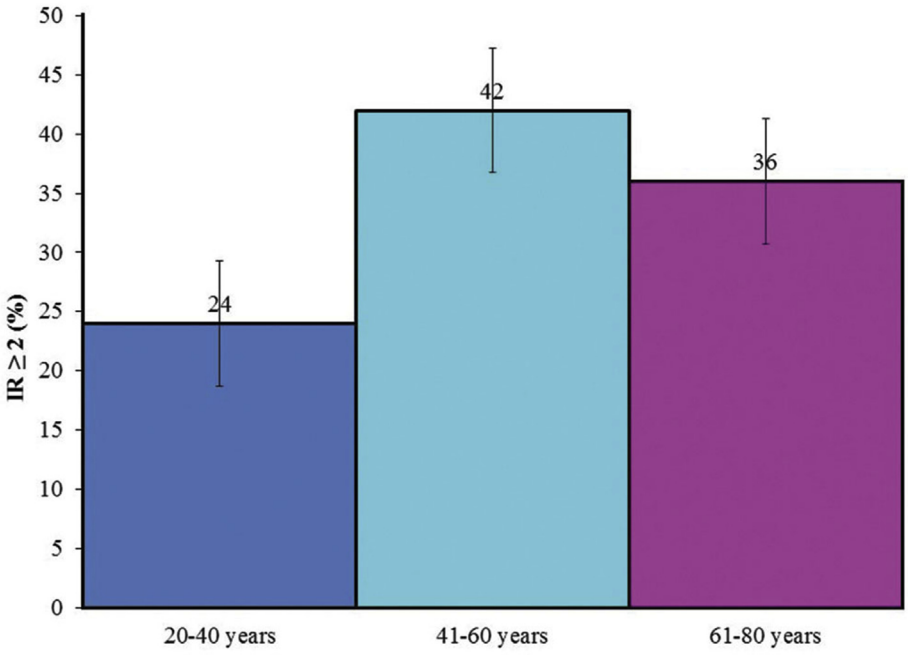

Fig. 2. Proportion of insulin resistance according to age groups.

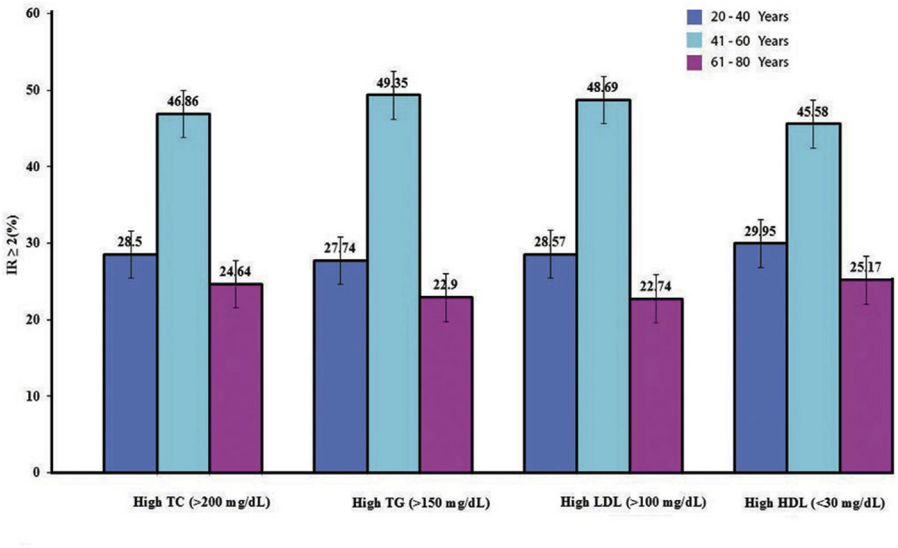

Fig. 3. Lipid profiles of insulin resistant subjects of three age groups.

Data in this study shows that group II subjects show characteristics of dyslipidemia. This finding explains several metabolic pathways may contribute to the insulin resistance [30]. So insulin resistance and obesity do not perform unique role for the altered lipid parameters. Many physiological concept and genetic determinants also reported previously [31–34]. We hope that within the next decade, scientific questions need to be addressed for us to have a more complete understanding of the relationship among obesity, blood lipids and obesity in Bangladeshi adults.

6. Conclusions

Genetic propensity to develop dyslipidemia, obesity and diabetes has been shown in South Asians but insulin resistance and the metabolic syndrome have been investigated poorly. We addressed two limitations within this investigation. Anthropometry is insufficient to determine healthiness and the application of statistical methods allow the filtering of accurate information. This research showed that serum lipoprotein ratios had significant positive correlation with insulin resistance, which could be used as simple, reliable, and economic biomarkers to evaluate insulin resistance.

Author contributions

Concept or design: SUF Malik, AK Azad.

Acquisition of data: SUF Malik.
Analysis or interpretation of data: SUF Malik, MS Islam.
Drafting of the article: SUF Malik, Z Mahmud, J Alam.
Critical revision for important intellectual content: SUF Malik, AK Azad.

Conflicts of interest

The authors have no conflicts of interest to disclose. 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.

Ethical approval

The research protocols for the use of human blood were approved by Ethical Review Board of North East Medical College and Hospital. Written informed consent was obtained from all participants.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.dsx.2018.10.015.

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