A Study to Assess and Correlate Serum Lipid Profile with Reaction Time in Healthy Individuals

Sagar Dua¹ · Praveen Singh¹ · Sarama Saha¹

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Abstract Dyslipidaemia, metabolic syndrome, diabetes mellitus and arterial hypertension contribute to the risk of cognitive disorder and dementia. However very few and conflicting results are available with respect to the impact of lipoprotein ratios on cognitive functions in healthy individuals. Therefore, this study was aimed to investigate the association of lipid profile and its ratios with reaction time in young healthy individuals. 89 individuals (54 male and 35 female) with mean age of 31.20 ± 3.19 years were selected for this observational study conducted at AIIMS Rishikesh and written consent was obtained. TC, TG, HDL were measured by semi auto analyzer following the manufacturers' instruction and LDL was calculated by Friedewald formula. Reaction time (simple and choice reaction time) was assessed using a software package, Deary–Liewald reaction time task. Association of various parameters was calculated by pearson's correlation coefficient using SPSS version 23.0. Reaction time showed significant negative association with BMI ($r = -0.323$, $p = 0.002$) in total study participants as well as with TG ($r = -0.440$, $p = 0.008$) and TG/HDL ($r = -0.402$, $p = 0.025$) in female individuals. From this study, it could be concluded that TG/HDL ratio, the superlative predictor of concomitant presence of cardiovascular disease, insulin resistance and metabolic syndrome may be considered as a biomarker for assessment of cognitive function in young healthy female individuals.

Keywords Simple reaction time · Dyslipidaemia · Lipid ratio · Choice reaction time · Deary–Liewald reaction time task

Introduction

Cerebral lipids specially cholesterol, play a crucial role in maintaining the homeostasis of neuronal membrane and synaptic function. Dyslipidaemia, is a metabolic abnormality leading to a persistent increase in the plasma concentration of total cholesterol (TC) and triglycerides (TG). It is a common cause of morbidity all over the world, and the most common form is hypercholesterolemia. It is estimated that hypercholesterolemia is responsible for 2.6 million (4.5%) deaths in the world. [1]. It has been documented that an increased level of total cholesterol and low-density lipoproteins contribute to the risk of mental disorders towards later part of life [2].

Dyslipidemia leads to increase in level of cerebral myo-inositol elevations in middle age. A recent study showed that increased myo-inositol affect negatively to memory performance in someone's middle of the age. Increase in myo-inositol occur early in the neurodegenerative process and predict cognitive decline in most of the conditions [3]. Moreover, in mild-to-moderate Alzheimer's disease, plasma TG and HDL cholesterol may have a role in maintaining blood brain barrier integrity [4].

This neurological involvement can be investigated by estimating reaction time which measures the time period between application of a stimulus and response by individual [5]. In obesity dyslipidaemia has been documented to play a major role in development of cerebral neurochemical alterations [3]. The significant effect of age, gender and body mass index on reaction time has already

✉ Sarama Saha
saramasaha@yahoo.co.in

¹ Department of Biochemistry, AIIMS, Rishikesh, India

been documented in Indian setting [6]. The correlation between atherosclerosis index (low-density lipoprotein (LDL)/HDL and TC/HDL) and reaction time have been documented in postmenopausal women with respect to APO E gene polymorphism [7]. Literature review reveals a conflicting finding on association of lipid profile and reaction time. However, the association of TG/HDL ratio, a physiologically relevant and practical index of concomitant presence of metabolic syndrome, insulin resistance and dyslipidaemia, with cognitive function in healthy young individuals has not been reported before. Moreover, it has been documented that the impact of TG/HDL changes as a function of race and ethnicity. Therefore, this study is aimed to investigate the correlation between lipid profile including TG/HDL ratio and reaction time in our setting among Uttarakhand populations which has not been explored before. This may give an insight into the impact of lipid metabolism on neurological deficit in young healthy individuals.

Study Design and Methodology

This observational study was conducted in 2018 from January to July at AIIMS Rishikesh on individuals aged 20–40 years having good general health.

The criteria for exclusion from this study were: patients with type I and 2 Diabetes mellitus and other endocrine or chronic diseases, motor impairment of upper limbs, iron deficiency anaemia, taking drugs like anti inflammatory drugs, antihistamines, caffeine & nicotine within 12 h before reaction time test, psychotropics, e.g. sedatives, hypnotics & tranquilizers, lipid lowering agents. The study was approved by the local ethics committee (IEC code; 108/IEC/UIS/2017) and written informed consent was obtained from all participants according to the guidelines of the institutional review boards for human studies at AIIMS Rishikesh. Anthropometric measurements such as waist circumference (using a measuring tape at the narrowest point between lowermost rib and the uppermost part of lateral border of right iliac crest), hip circumference (by measuring tape), weight (using a digital balance in minimal clothing) and height (using a stadiometer) were carried out. Body mass index (BMI) was calculated using the Quetelet's index: weight (kg)/height (m²). Seated blood pressure was recorded by a trained nurse after the patient has rested for 5 min. Blood samples were collected after an overnight fast from all willing participants (n = 89). Plasma lipids/lipoproteins (TC: cholesterol oxidase peroxidase (CHO-POD method, TG: glycerophosphate oxidase peroxidase (GPO-POD method), HDL: enzymatic immunoinhibition) were measured by a semiautomatic biochemistry analyzer (Erba, Mannheim, Germany) using commercially available

diagnostic kits (Erba, Germany). LDL was calculated by Friedewald formula:

$$\text{LDL} - \text{C} = [\text{Total cholesterol}] - [\text{HDL} - \text{C}] - [\text{TG}]/5.$$

Serum cholesterol to lipid (TC/HDL, TG/HDL, LDL/HDL) ratio was calculated.

Choice reaction time & simple reaction time were assessed using Deary–Liewald reaction time task [8], a software package in which four white squares, corresponding to the four keys on a standard computer keyboard, are displayed on the middle of the computer screen. The laboratory environment was kept quiet with temperature between 20 °C and 25 °C. In order to get accurate results patients were instructed to practice several times.

Statistical Analysis

Statistical analysis was carried out using the software package SPSS 23.0. Normality distribution of the data was checked. In the characteristics of the study sample, lipid levels and reaction time (standardized results) arithmetic means were calculated [Mean (M) ± standard deviation (SD)], for quantitative characteristics and relative numbers (%) were calculated for qualitative characteristics. The significance of the differences in quantitative characteristics between male and female groups was calculated using independent student t test. To investigate correlations between cognitive functions (reaction time) and lipid level Pearson's correlation coefficient (r) and linear regression analysis were used.

Results

The study comprised of 89 individuals, of which 54 (61%) were male and 35 (39%) were female. Almost all participants had high school education and female participants had comparatively higher education compared to male. Table 1 presents their characteristics. The mean age of total participants in the study was 31.20 ± 3.19 years. The mean BMI value was 21.55 ± 4.27 kg/m². The average simple reaction time and choice reaction time was 293.46 ± 31.32 ms and 524.27 ± 146.68 ms respectively. The mean value of total cholesterol (161.6 ± 9.52) mg/dl, HDL cholesterol (56.8 ± 15.72) mg/dl, LDL cholesterol (89.0 ± 14.42) mg/dl, and TG (80.8 ± 28.03 mg/dl) were within reference range. Table 2 represents the compilation of demographic profile and the results of analysis of lipid profile in males and females separately. There was no significant difference between males and females with respect to age, BMI, reaction time and lipid profile data except LDL. However, males (SRT 379.313 ± 124.4388 ms and CRT 554.194 ± 146.05 ms)

Table 1 Characteristic features of total study participants

Parameters	Mean $\pm$ SD
Total participants	89 (54 M + 35 F)
Age (years)	31.20 $\pm$ 3.19
Waist/hip	0.99 $\pm$ 0.02
Waist circumference (cm)	79.6 $\pm$ 21.81
Blood glucose (mg/dl)	84.2 $\pm$ 6.90
Urea (mg/dl)	19.0 $\pm$ 2.91
Creatinine (mg/dl)	0.74 $\pm$ 0.01
TC (mg/dl)	161.6 $\pm$ 9.52
HDL (mg/dl)	56.8 $\pm$ 15.72
LDL (mg/dl)	89.0 $\pm$ 14.42
TG (mg/dl)	80.8 $\pm$ 28.03
TC/HDL	3.01 $\pm$ 0.79
LDL/HDL	1.72 $\pm$ 0.74
TG/HDL	1.12 $\pm$ 0.65
BMI	21.55 $\pm$ 4.27
Simple reaction time (ms)	293.46 $\pm$ 31.32
Choice reaction time (ms)	524.27 $\pm$ 146.68

had faster reaction time than females (SRT 408.126 $\pm$ 172.33598 ms and CRT 603.436 $\pm$ 216.87 ms).

Tables 3, 4, and 5 represents the association of simple reaction time with lipid profile of total study participants, male and female participants respectively. BMI showed a significant negative association with SRT in total study

Table 3 Correlation with simple reaction time (SRT) for total study participants

Variable	Correlation coefficients	P
Waist/hip	– .145	.181
Waist circumference	– .077	.481
BMI	.234*	0.029
TC	– .066	.544
HDL	– .066	.546
LDL	– .068	.531
TG	.069	.528
TG/HDL	.142	.201
LDL/HDL	– .066	.555
TC/HDL	– .026	.814

*P value < 0.05 is significant

participants ($r = .234^*$, $p = 0.029$). In case of male and female participants, although there was no significant association between these two parameters, it maintained the negative trend. However, in case of female participants waist/hip ratio showed a significant negative association ($r = -.343$, $p = 0.044$). Moreover, in case of female individuals, TG and TG/HDL ratio showed a negative association with SRT though it was not significant.

Correlation between choice reaction time and lipid profile parameters of total study participants, male and female individuals have been presented in Tables 6, 7, and 8. BMI showed a significant negative association with CRT

Table 2 Characteristic features of male and female participants

Variable	Male	Female	Significance
Number	54	35	
Age	31.85 $\pm$ 5.286	33.26 $\pm$ 7.358	.298
Height (cm)	168.48741 $\pm$ 7.422561	158.97817 $\pm$ 6.183191	.000
Weight (kg)	72.20 $\pm$ 10.781	61.09 $\pm$ 9.240	.000
Hip circ (cm)	95.2159 $\pm$ 10.69799	91.1829 $\pm$ 11.36944	.094
Waist/hip	.9374 $\pm$ 0.049	.9593 $\pm$.056	.058
Waist circumference (cm)	89.3641 $\pm$ 12.09031	87.2657 $\pm$ 10.70433	.406
BMI	25.391 $\pm$ 3.19	24.21 $\pm$ 3.611	.110
HDL (mg/dl)	38.685 $\pm$ 6.2580	40.874 $\pm$ 8.9298	.177
LDL (mg/dl)	119.889 $\pm$ 26.8815	103.434 $\pm$ 23.9635	.004
TG (mg/dl)	92.52 $\pm$ 36.579	91.83 $\pm$ 40.691	.934
TC (mg/dl)	177.02 $\pm$ 28.06	165.80 $\pm$ 24.861	.057
Simple reaction time SRT (ms)	379.313 $\pm$ 124.4388	408.126 $\pm$ 172.3359	.368
Choice reaction time CRT (ms)	554.194 $\pm$ 146.05	603.436 $\pm$ 216.87	.209
TG/HDL	2.4703 $\pm$ 1.246	2.4065 $\pm$ 1.290	.823
LDL/HDL	3.1542 $\pm$.777	2.659 $\pm$.8328	.007
TC/HDL	4.6380 $\pm$.8232	4.228 $\pm$.9194	.038

*P value < 0.05 is significant

Table 4 Correlation with simple reaction time (SRT) for male participants

Variable	Correlation coefficients	Significance
Hip circumference	− .042	.766
Waist/hip	− .197	.161
Waist circumference	− .187	.183
BMI	− .012	.935
TC	.005	.974
HDL	− .040	.780
LDL	.014	.919
TG	.273	.050
TG/HDL	.260	.063
LDL/HDL	− .079	.576
TC/HDL	− .081	.569

**P* value < 0.05 is significant

Table 5 Correlation with simple reaction time (SRT) for female participants

Variable	Correlation coefficients	Significance
Hip circumference	.307	.073
Waist/hip	− .343*	.044
Waist circumference	.128	.465
BMI	− .048	.782
TC	− .012	.947
HDL	− .027	.876
LDL	− .034	.845
TG	− .179	.305
TG/HDL	− .025	.893
LDL/HDL	.026	.119
TC/HDL	.891	.523

**P* value < 0.05 is significant

among total study participants but not in male and female participants (when considered separately). Moreover, in female participants, TG ($r = -.440^*$; $p = 0.008$) and TG/HDL ($r = -.402^*$; $p = 0.025$) showed a significant negative association with CRT. This significance persisted even after adjustment with age and BMI. However, other lipid ratios did not show significant association with reaction time (SRT and CRT) in study participants.

Discussion

The pathological processes of cognitive disorders may begin several years before the appearance of the clinical manifestation [9] and once it is developed, it becomes

Table 6 Correlations with choice reaction time (CRT) for total study participants

Variable	Correlation coefficients	Significance
Waist/hip	− .085	.436
Waist circumference	− .131	.228
BMI	− .323**	.002
TC	− .196	.069
HDL	− .022	.841
LDL	− .111	.307
TG	− .209	.052
TG/HDL	− .199	.071
LDL/HDL	− .116	.298
TC/HDL	− .177	.110

**P* value < 0.05 is significant

Table 7 Correlations with choice reaction time (CRT) for male participants

Variable	Correlation coefficients	Significance
Hip circumference	− .254	.069
Waist/hip	− .014	.923
Waist circumference	− .216	.124
BMI	− .147	.298
TC	− .006	.967
HDL	− .056	.695
LDL	− .036	.799
TG	.106	.455
TG/HDL	.193	.171
LDL/HDL	− .090	.524
TC/HDL	− .047	.740

**P* value < 0.05 is significant

irreversible. The detection of an elevated risk at the earliest possible time may bring about the possibilities of early initiation of treatment and the prophylaxis of cognitive disorders. Given the epidemic of neurodegenerative disorders, there is a need to identify a simple and inexpensive clinical tool that would help the physicians for early identification of concomitant presence of cardiovascular problems, insulin resistance and cognitive dysfunctions in healthy individuals. Hence this study was conducted to explore the possible existence of a relationship between the serum lipid profile including lipoprotein ratios (LDL/HDL, TC/HDL and TG/HDL) and the reaction time (SRT and CRT), as a measure of cognitive ability, in healthy individuals [9].

Our study revealed a negative association with BMI which indicates that the within reference value of BMI,

Table 8 Correlations with choice reaction time (CRT) for female participants

Variable	Correlation coefficients	Significance
Hip circumference	– .040	.821
Waist/hip	– .213	.220
Waist circumference	– .110	.529
BMI	– .223	.197
TC	– .315	.065
HDL	– .029	.868
LDL	– .289	.092
TG	– .440**	.008
TG/HDL	– .402*	.025
LDL/HDL	– .201	.277
TC/HDL	– .278	.130

**P* value < 0.05 is significant

individuals with higher BMI level have faster reaction time. It is in concordance with a previous study on healthy young females conducted by Nene et al. [10]. They showed that the visual reaction time was significantly prolonged in subjects having lower BMI. This study indicates that within the reference range, higher BMI has a supportive effect on sensory motor association.

The present study demonstrated that there was a significant association with TG but not with LDL/HDL and TC/HDL ratio with reaction time which is in agreement with previous study conducted by Bojar et al. [7]. They explained this effect by reporting that these ratios do not, but TG significantly depend on APO E gene polymorphism which is confirmed to be a high-risk factor for the development of cognitive disorders.

Inverse correlation of serum TG levels with executive function is in favor of previous study conducted by Parthasarathy et al. [11] on nondemented elderly adults after controlling for age. In women, low TG levels had been shown to predict better verbal ability performance prior to 65 years of age and markedly better maintenance of verbal ability. Similarly, in men, lower TG levels predicted better performance and slower decline in general cognitive ability before 65 years of age [12]. Yin et al. [13] also concluded that the high normal plasma TG helps in preservation of cognitive function in Chinese oldest-old. This implies that higher normal concentrations of TG are protective for cognitive function, while a pathological concentration of TG may outweigh these beneficial effects. This protective effect of TG may be attributed to increase in blood brain barrier transport of ghrelin and insulin that have positive effects on cognition [14, 15] and improve the brain's integrity and performance by increasing circulating free fatty acids [16].

Our study revealed a significant negative association of TG/HDL ratio with reaction time in female participants. However, in previous studies, higher HDL and lower TG had been documented to predict better maintenance of cognitive abilities [12]. This discrepancy of findings may be explained because of different study setting. Our study participants compared to the other study, were of younger healthy individuals having TG and HDL levels within normal limits that has a protective effect on cognitive functions [13] while the pathological concentration of TG that was considered in other studies may induce neurological deficit by accelerating the formation of atherosclerotic lesions resulting in prolonged reaction time.

The generalizability of the study results would be limited because of its small sample size. Thus, a further study with a larger sample size and taking into consideration of the expression of APOE gene polymorphism would be warranted in future for establishing its clinical implication.

Conclusion

From this study, it could be concluded that in young healthy individuals (20–40 years) BMI, TG and TG/HDL ratio have significant negative association with reaction time that is an important indicator of processing capabilities of central nervous system. TG/HDL ratio, the superlative predictor of concomitant presence of cardiovascular disease, insulin resistance and metabolic syndrome may be considered as a biomarker for assessment of cognitive function in young female healthy individuals.

Compliance with Ethical Standards

Conflict of interest The authors state that there is no conflict of interest and they have nothing to declare.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the AIIMS Rishikesh (Reference number: 108/IEC/UIS/2017) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent The written informed consent was obtained from all individuals according to the guidelines of the institutional review boards for human studies at AIIMS Rishikesh.

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