

GABRA6 and SLC6A4 genotypes are correlated with the fasting blood glucose and physical fitness in the seemingly healthy young adults

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ABSTRACT

Introduction: We examined environmental and genetic factors potentially correlated with the blood glucose and physical fitness in Kediri, East Java, Indonesia to elucidate the predominant cardiovascular disease risk.

Methods: This was a cross-sectional study on 68 adults aged 18-22 years. Direct interview was conducted to get socio-economy, daily diets (rice/ R, snacks and sweets/ SS, veggies and fruits/ VF), daily activity (locomotors and non-locomotors) data. Peripheral blood-GABRA6 and SLC6A4 polymorphisms, fasting blood glucose (FBG), blood pressure, 3 fitness parameters (1 min push-up, 3 minutes step up, pulse rate after 3 minutes step-up) were measured by 2 independent and pre-trained medical doctors. Kruskal-Wallis, Chi-Square, and eta-coefficient tests were used to seek differences between genotypes and correlation strength between variables, respectively (significant if $p < 0.05$).

Results: Both gene's genotypes showed significant correlations with the FBG ($p=0.042$, $p=0.013$, respectively); GABRA6 polymorphism significantly correlated with SU ($p=0.033$). There was a significant difference in the FBG between 2 VF subgroups ($p=0.02$). Strongest association was found between FBG and SLC6A4 ($\eta=0.3$); PR and GABRA6 ($\eta=0.168$), PU and SLC6A4 ($\eta=0.38$); SU and Locomotors ($\eta=0.237$).

Conclusions: In these seemingly healthy young adults, daily diets and the genotypes of both genes have a good association with the FBG and physical fitness levels.

Keywords: diabetes mellitus, fitness, GABA, health risk, serotonin

Introduction

Pre-diabetes and hypertension would increase risk to develop metabolic disease including type 2 diabetes mellitus characterized by relative decreased insulin secretion and insulin resistance that constituting for approximately more than 90% of all diabetes cases (Qiu

et al., [2015](#); Hadi Alijanvand et al., [2020](#); Kalanjati et al., [2021](#)). The prevalence of T2DM and pre-diabetes have been increased worldwide, and reported to widely associate with an increase prevalence of cardiovascular diseases (CVD) including hypertension (Chia et al., [2020](#)). The prevalence of diabetes for all age groups was

approximately 2.8% in 2000 and will be around 4.4% in 2030 globally (Hakola, 2015; Hamasaki, 2016; NCD Risk Factor Collaboration (NCD-RisC), 2016). This could become a national burden, and is warranted for early detection and prevention. Management of pre-diabetes and pre-hypertension including changes in lifestyle and monitoring glycaemia also sodium intake to lower the risk of developing diabetes and CVD in the later life (Hamasaki 2016; Kamal et al 2020; Mathur et al. 2021).

Physical activity was reported to correlate with the levels of blood glucose (Osailan et al., 2021). Blood glucose also determines the health and physical fitness that normal levels would be allowing individuals to carry out daily activity without excessive fatigue. Amongst many factors determining the levels of physical fitness i.e. muscular strength, endurance, and flexibility as needed to perform sit-up and push up exercises (Hakola, 2015). It was reported that physical fitness can be used to assess university student's study performance (Sookhanaphibarn and Choensawat, 2015). Physical activity and low-carbohydrate diets improve glycemic control and decrease the risk of CVD and mortality rate in pre-diabetes patients with hypertension. Moderate to high-intensity exercise is recommended in controlling the glycemic levels and increasing the insulin sensitivity, however in certain cases walking for at least 30 minutes a day has been reported to reduce the T2DM risk by approximately 50% (Hakola 2015; Hamasaki 2016; Kam et al 2020). On the other hand, sedentary time was reported to have a close association with higher risk of diabetes and CVD incidence and mortality rate in adults (Biswas et al 2015).

On the other hand, the genotypes of SLC6A4 (Serotonin transporter gene, solute carrier family 6 member 4), which code serotonin transporters have been reported to associate with body mass index (BMI) and situation awareness performance in healthy young adults in Colombia (González-Giraldo et al., 2018). Serotonin uptake affects the mood and behavior through its work at the limbic system and hypothalamus (Dunn et al., 2012; González-Giraldo et al., 2018). This neurotransmission accounted for appetite, autonomic signals to regulate the blood pressure, emotion and higher cortical functions related to the hypothalamus,

limbic system and the prefrontal cortex (Qin et al., 2018; Simpson et al., 2008). In these area, gamma-amino butyric acid (GABA) has been observed to play major role as the predominant inhibitory neurotransmitter, and closely related with the stress response, specifically in obese persons (Arias et al., 2012; Lynch et al., 2015; Rosmond et al., 2002). GABRA6 (gamma amino-butyric acid type A receptor subunit alpha-6) gene polymorphism has been reported to correlate strongly with mood, anxiety and motor response; this gene encodes the GABA-A alpha-6 subunit protein receptors (Han et al., 2008; García-Martín et al., 2018). Although both neurotransmissions have been shown to relate with feeding behavior, stress response and lipid deposition, their impact on the blood glucose and other determinants of CVDs have yet widely explored and thus examined in the current study. The result of this study would provide evidence on the association of genetic and non-genetic determinants with the physical performance and risk factors to develop CVDs in later life.

Materials and Methods.

This study was carried out in accordance with the Declaration of Helsinki. All participants in this study signed written informed consents and this study has been granted by the health ethical committee (No. 226/EC/KEPK/FKUA/2020). We conducted an observational analytic study with a cross-sectional design to analyze the daily diets and activity, biomarkers and the genotypes of GABRA6 and SLC6A4 with the physical fitness of 68 consented participants aged 18-22 years old Javanese ethnicity males and females conducted in March-April 2020. All measurements were done in duplicate by 2 independent-pre trained medical doctors for minimizing any potential observer bias. We have done a preliminary study to ensure standard protocols can be applied thoroughly during the observation. We include participants with the current healthy condition and able, also willing to follow all protocols in this study. We exclude ones who have a history of any metabolic diseases i.e. type-2 diabetes mellitus, dyslipidemia and any cardiovascular diseases. We also exclude those with history of any major known

Table I Frequency of SLC6A4 and GABRA6 polymorphisms

Gene	Genotype	n	Frequency	Allele	n	Frequency	P Chi-Square test
SLC6A4	S/S	51	0.75	S	116	0.85	2.19 (p>0.05)
	L/S	14	0.21	L	20	0.15	
	L/L	3	0.04				
GABRA6	T/T	32	0.47	T	98	0.72	3.97 (>0.05)
	T/NT	34	0.5	NT	38	0.28	
	NT/NT	2	0.03				

diseases i.e. any type of neoplasms, major injury and autoimmune diseases. Information from each participant i.e. daily diet including approximate rice consumption (Rice) in a day (100 grams, 200 grams, ≥ 300 grams), vegetables and fruit (Veggies-Fruits) inclusion in daily diet (yes or no), daily sweets and snacks (Snacks-Sweets) consumption (yes or no); non-locomotors activity was measured from daily gadget usage (less than 30 minutes, 30 to 120 minutes, 120 to 240 minutes and more than 240 minutes); data of daily walking time/ locomotor (less than 45 minutes, 45 to 120 minutes, more than 120 minutes), age, family monthly income were also collected via direct interview (Biswas et al., 2015; Castro, Macedo-de la Concha and Pantoja-Meléndez 2017; Castro-Diehl et al., 2014). The age of each participant was confirmed from the data in the citizen card. Blood pressure was measured in participants in sitting position prior to other tests, after 5 minutes of rest at the time of survey, using digital

sphygmomanometer (HEM-7121, China) after checking for the device accuracy by comparing with the measurement through a mercury sphygmomanometer. The prehypertension blood pressure was defined by $120 \text{ mmHg} < \text{SBP} < 139 \text{ mmHg}$ and/ or $80 \text{ mmHg} < \text{DBP} < 89 \text{ mmHg}$. Hypertension blood pressure was defined by $\text{SBP} \geq 140 \text{ mmHg}$ and/ or $\text{DBP} \geq 90$ or if the patient was under antihypertensive drugs (Hadi Alijanvand et al., 2020). The fasting blood glucose (FBG) was analyzed using the Easy-Touch machine (Taiwan) by applying peripheral blood from the fingertip, after a 12-hour overnight fast. The FBG levels $70\text{-}100 \text{ mg/dL}$ was classified as normal, $>100\text{-}125 \text{ mg/dL}$ was classified as pre-diabetes (Chia et al., 2020; Hadi Alijanvand et al., 2020). The cardiovascular fitness were evaluated from the numbers of 1 minute push-up and 3 minutes step-up (PU and SU, respectively) were counted with resting intervals of 60 minutes, and the pulse rate after SU (PR) was measured subsequently (Sookhanaphibarn and Choensawat 2015). All parameters were measured by 2 medical doctors trained prior to the current study for standardized procedures. The average from two closest measurements of each variable were used.

The isolated DNA was obtained from 68 participants (from a peripheral blood-swab). The DNA was extracted using the DNA extraction kit (Instagene Matrix, BioRad, USA). The spectroscopy was done to quantify the DNA concentration (FluoStar Omega, BMG Labtech, Germany). The primer pair of SLC6A4 was 5'-TCC TCC GCT TTG GCG CCT CTT CC-3' and 5'-TGG GGG TTG CAG GGG AGA TCC TG-3' (González-Giraldo et al., 2018; González-Giraldo et al., 2018). The primer pair of GABA-a receptor subunit $\alpha 6$ (GABRA6) was 5'-GGA GGC ACC AGT AAA ATA GAC CAG-3' and 5'-AAT ACT GAA CAA TGG AAG ACA AAA-3' (García-Martín et al., 2018; Rosmond et al., 2002; Uhart et al., 2004). The PCR was done using 2x Go TagGreen master mix PCR (Promega) on a thermocycler (TC-5000, Techne, UK) in $20 \mu\text{l}$ of total reaction volume, contained 20 ng genomic DNA as template. The PCR reaction was set as follows: pre-denaturation at 95°C for 5 minutes, followed by reaction cycles of denaturation step at 94°C for 30 seconds, and elongation at 72°C for 40 seconds, and ended with post-elongation at 72°C for 10 minutes. For GABRA6 analysis, the next step was digestion of PCR product using AlwNI restriction enzyme (NEB) according to the NEB product manual (Han et al., 2008; Lynch et al., 2015). The digestion fragment size was determined after separation on agarose gel. The electrophoresis was done using 12% agarose gel containing ethidium bromide, and then were visualized on the UV box (BioDocAnalyze, Swiss). The approximate restriction

Table 2 Characteristics of the socioeconomic, environmental and health parameters of all participants (N=68)

No.	Variables	n (%)
1	Gender	
	Male	32 (47.1)
	Female	36 (52.9)
2	Age (years)	
	18	1 (1.5)
	19	10 (14.7)
	20	16 (23.5)
	21	29 (42.6)
	22	12 (17.6)
3	Family monthly income (IDR)	
	< 2 millions	3 (4.4)
	2-5 millions	46 (67.6)
	>5-10 millions	15 (22.1)
	>10 millions	4 (5.9)
4	Non-genetic determinants	
A	Daily walking time (locomotors activity)	
	<45 minutes	47 (69.1)
	45-120 minutes	15 (22.1)
	>120 minutes	6 (8.8)
B	Daily use of gadget time (non-locomotors)	
	<30 minutes	2 (2.9)
	30-120 minutes	24 (35.3)
	120-240 minutes	20 (29.4)
	>240 minutes	22 (32.4)
C	Daily rice intake (grams)	
	<100	24 (35.3)
	100-200	29 (42.6)
	200-300	15 (22.1)
	>300	0 (0)
D	Daily snacks and sweets intake	
	Yes	47 (69.1)
	No	21 (30.9)
E	Daily veggies and fruits intake	
	Yes	16 (23.5)
	No	52 (76.5)
5	Blood pressure	
	Normal	48 (70.6)
	Pre-hypertension	17 (25)
	Hypertension	3 (4.4)
6	Fasting blood glucose (mg/dL)	
	Normal	64 (94.1)
	Pre-diabetes	4 (5.9)
	Diabetes	0 (0)

Table 3 Differences in the blood pressure, FBG and physical fitness amongst SLC6A4 genotypes, GABRA6 genotypes, daily diets and activities subgroups

Groups	Blood Pressure		FBG (mg/dL)		Physical Fitness					
					Pulse rate after 3 minute step-up		Count of 1 minute push-up		Count of 3 minute step-up	
	P Kruskal-Wallis	P Chi-Square	P Kruskal-Wallis	P Chi-Square	P Kruskal-Wallis	P Chi-Square	P Kruskal-Wallis	P Chi-Square	P Kruskal-Wallis	P Chi-Square
SLC6A4	.996	.967	.381	.042*	.592	.211	.708	.335	.594	.947
GABRA6	.755	.877	.525	.013*	.280	.702	.461	.956	.523	.033*
Locomotors	.224	.266	.074	.271	.678	.902	.388	.59	.105	.051
Non- Locomotors	.716	.900	.431	.451	.816	.491	.753	.935	.906	.888
Rice	.706	.664	.200	.582	.777	.289	.795	.728	.373	.511
Snacks- Sweets	.802	.473	.099	.738	.729	.393	.609	.506	.627	.635
Veggies-Fruits	.084	.215	.016*	.493	.954	.048*	.648	.501	.582	.741

fragment length of GABRA6 T-allele was 423 base pairs and the non-T allele were 257 and 166 base pairs; whilst the SLC6A4 L-allele was 512 base pairs and S- allele was 469 base pairs. Fasting sub-sample for the PCR was used ($\pm 10\%$ of population) to confirm the genotype of each polymorphism. The distribution of individual genotype and frequency of the participants and control subjects were analyzed using Hardy-Weinberg Equilibrium calculator. Kolmogorov-Smirnov tests was used for normality test. Differences in the blood pressure, FBG and physical fitness between SLC6A4 genotypes, GABRA6 genotypes, daily diets and activity subgroups were assessed using Kruskal-Wallis and Chi-Square tests. Differences in genotype frequencies were assessed using the Chi-Square test. Pearson's' Chi-Square correlation was used to measure the significance of correlation of the SLC6A4 genotypes; GABRA6 genotypes; daily diets and activity subgroups with the blood pressure, whilst Eta-coefficient test was used to assessed the degree of association of the SLC6A4 genotypes; GABRA6 genotypes; daily diets and activity subgroups with the FBG and physical fitness parameters. A two-tailed $p < 0.05$ was considered statistically

significant (IBM SPSS Statistical Package Version 17.0, USA).

Results

There were 32 (47.1%) males and 36 (52.9%) females participating in this study. Approximately The mean age was 20.7 ± 0.99 years with predominant family monthly income was between 2-5 million IDR (46%). Daily activity of non-locomotors and locomotors mostly consisted of less than 45 minutes of walking (47%) and more than 30 minutes of using gadgets (97.1%; $n=66$). Whereas the daily diets consisted of more than 300 grams of rice was found in 22.1% of all participants; 69.1% had snacks and sweets whilst 76.5% had not veggies and fruits in their daily routine (Table 2).

We observed 3 polymorphism of SLC6A4 gene i.e. L/L, L/S, S/S; and 3 polymorphism of GABRA6 gene i.e. (T/T, T/NT, NT/NT) (Figure 1a-b). The distribution of L and S alleles of SLC6A4 and of T and NT alleles of GABRA6 followed the Hardy-Weinberg equilibrium. The frequency of L and S allele of SLC6A4 was 0.15% and 0.85%, with $p > 0.05$, respectively; whilst the frequency of T and NT allele of GABRA6 was 0.72% and 0.28%, with

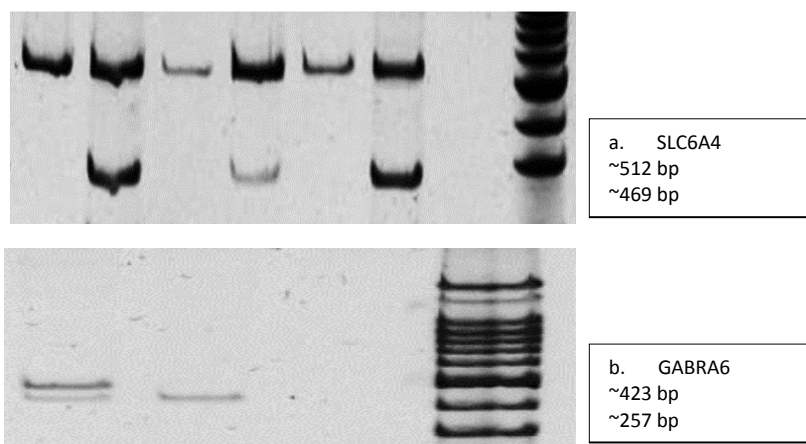


Figure 1 a-b. A representative gel of SLC6A4 showed 2 distinctive alleles i.e., L-allele (~512 base pairs) and S-allele (~469 base pairs); whilst GABRA6 showed 2 distinctive bands i.e., T-allele (~423 base pairs) and non-T/ C-allele (~257 base pairs).

$p > 0.05$, respectively. The frequency of SLC6A4 L/L, L/S and S/S was 0.04%, 0.21% and 0.75%, respectively; whilst GABRA6 T/T, T/NT and NT/NT was 0.47%, 0.5% and 0.03%, respectively (Table 1).

The fasting blood glucose (FBG) was found normal in 94.1% participants, whilst 5.9% was pre-diabetes with FBG levels was ≥ 100 mg/dL. The blood pressure was categorized normal-tension in 70.6%, pre-hypertension in 25% and hypertension with systole/ diastole pressure was $\geq 140/90$ mmHg in 4.4%.

We found no significant differences either on the blood pressure, FBG, physical fitness [PR, PU, SU], between 3 groups of SLC6A4 polymorphisms ($p=0.996$, $p=0.381$, [$p=0.592$, $p=0.708$, $p=0.594$]), and between 3 groups of GABRA6 polymorphisms ($p=0.775$, $p=0.525$, [$p=0.28$, $p=0.461$, $p=0.523$]), respectively. We found no significant differences either on the blood pressure, FBG or 3 physical fitness parameters [PR, PU, SU] amongst: (1) 3 groups with different quantity of daily rice intake ($p=0.706$, $p=0.2$, [$p=0.78$, $p=0.8$, $p=0.63$]); (2) 2 groups of snacks and sweets daily intake ($p=0.802$, $p=0.099$, [$p=0.73$, $p=0.61$, $p=0.58$]); (3) 3 groups of locomotors daily activity time ($p=0.224$, $p=0.074$, [$p=0.68$, $p=0.39$, $p=0.11$]); and (4) 4 groups of non-locomotors daily activity time ($p=0.716$, $p=0.431$, [$p=0.82$, $p=0.75$, $p=0.91$]), respectively. Although there were no significant differences on the blood pressure ($p=0.08$), or on the physical fitness [PR ($p=0.95$), PU ($p=0.65$), SU ($p=0.58$)]; **the FBG between those who include and exclude veggies and fruits from their daily diets was significantly different ($p=0.02$) (Table 3).**

We found no significant correlations between SLC6A4 polymorphism either with the blood pressure ($p=0.97$), or with the physical fitness [PR ($p=0.21$), PU ($p=0.34$), SU ($p=0.95$)]; **however significant correlation was found with FBG ($p=0.042$).** We found no significant correlations between GABRA6 polymorphism either with the blood pressure ($p=0.88$), or with 2 physical fitness parameters [PR ($p=0.702$), PU ($p=0.96$)]; **however significant correlation was found with the SU ($p=0.033$) and with the FBG ($p=0.013$).** We found **significant correlations between diastole and non-locomotors activity daily ($p=0.005$); and between the PR and daily intake of veggies and fruits ($p=0.048$).** However no other significant correlations were observed either between the daily diets and the blood pressure, FBG or physical fitness; or between the daily activity time and these 3 cardiovascular risk factors (Table 3). **The highest eta-coefficient in the FBG was shown with the SLC6A4 genotypes ($\eta=0.3$); whilst in the physical fitness parameters [PR, PU, SU] was with the GABRA6 genotypes, with the SLC6A4 genotypes**

and with the daily locomotors activity ($\eta=0.168$, $\eta=0.38$, $\eta=0.237$, respectively) (Table 4).

Discussions

We found that the participants of this study were university students of the same race, and came from the low to middle class of family income. We also found that several of these seemingly healthy young adults suffered from the pre-diabetes and/ or pre-hypertension. Socioeconomic factors play a significant role to determine the utilization of healthcare and education, including cardiovascular-related preventive care (Mulyanto et al., 2019; Nadasya et al., 2021; NCD Risk Factor Collaboration (NCD-RisC) 2016). Castro-Diehl et al., (2014) reported variations in the correlations of income-wealth index and education with the cortisol levels (Castro et al., 2017). In African Americans race, this association tended to be strongest; it was reported that the income-wealth index showed contrast levels with the urinary stress hormones i.e. levels of cortisol,

Table 4. Association analysis of association degree between the blood pressure, FBG and 3 physical fitness parameters either with the SLC6A4 and GABRA6 genotypes or with the daily diets and activities

Dependent Variables	Independent Variables	P Pearson's Chi-Square test	Eta-Value (η^2)
BP	SLC6A4 genotypes	.967	-
	GABRA6 genotypes	.877	
	Rice	.644	
	Snacks_Sweets	.473	
	Veggies_Fruits	.215	
	Locomotors	.266	
	Non-Locomotors	.900	
	[FBG]	SLC6A4 genotypes	-
GABRA6 genotypes			.141
Rice			.191
Snacks_Sweets			.203
Veggies_Fruits			.274
Locomotors			.234
Non-Locomotors			.175
PR		SLC6A4 genotypes	-
	GABRA6 genotypes		.168
	Rice		.069
	Snacks_Sweets		.064
	Veggies_Fruits		.016
	Locomotors		.103
	Non-Locomotors		.151
	PU	SLC6A4 genotypes	-
GABRA6 genotypes			.036
Rice			.158
Snacks_Sweets			.132
Veggies_Fruits			.002
Locomotors			.037
Non-Locomotors			.100
SU		SLC6A4 genotypes	-
	GABRA6 genotypes		.134
	Rice		.173
	Snacks_Sweets		.070
	Veggies_Fruits		.063
	Locomotors		.237
	Non-Locomotors		.103

epinephrine, norepinephrine and dopamine; lower stress level was found amongst higher income-wealth group (Castro et al., [2017](#)).

In our study, the genotypes of both genes showed significant correlations with the fasting blood glucose, although stronger association was shown with the SLC6A4 compared to the GABRA6 genotypes. We also found that SLC6A4 and GABRA6 polymorphism had significant correlation with physical fitness. Stress response has been reported to be associated with the polymorphism of serotonin transporter gene's polymorphism, the SLC6A4. SLC6A4 plays a vital role in the reuptake of serotonin in the synaptic cleft, where this neurotransmitter can be found abundance both in the brain area controlling appetite and mood, also in the intestine where the digestion process actively occurs (García-Martín et al., [2018](#); González-Giraldo et al., [2018](#)). Mental status and motor response during various stressor induction have also been reported to correlate with the GABRA6 genotypes (Braat and Kooy [2015](#); Lynch et al., [2015](#)). GABRA6 is responsible for the expression of GABA-A alpha-6 receptors; this gene is located on chromosome 5q31.1-q35 (Rosmond et al., [2002](#)). By acting through this receptor, GABA (gamma-amino butyric acid) might affect the hormonal control of cortisol by reducing the secretion of corticotropin releasing hormone, which in turn increases the secretion of cortisol by the adrenal cortex. GABA is the predominant inhibitory neurotransmitter in the adult mammalian brain (Kalanjati et al., [2017](#); Miller et al., [2017](#); Qin et al., [2018](#)). Several natural diets component i.e. lithium, taurine, vitamin B6, vitamin B12 and folic acid from fermented milk products and/ or sprouts brown rice, barley and beans could raise the activity of GABA-ergic system. Gene alteration in GABA-A receptors have been shown to associate widely with the neurodevelopmental disorders due to the predominant inhibition modality in adult mammalian brain (Kalanjati et al., [2017](#); Rosmond et al., [2002](#); Uhart et al., [2004](#)). GABRA6 polymorphism correlates with abdominal obesity and cortisol secretion that leads to hypercortisolism. Environmental determinants including stress produce modulation on the GABA-hypothalamic-pituitary-adrenal systems in the individuals with genetic vulnerability. Polymorphism of GABRA6 alleles also associated with specific psychoneurological traits i.e. neuroticism, motor reflex response and mood disorders in women (Chiriboga et al., [2008](#); Han et al., [2008](#); Lynch et al., [2015](#)). Arias et al., ([2012](#)) reported that neuroticism as shown as harm avoidance traits connected to the anxiety, self-consciousness,

vulnerability and depression in persons with homozygous T allele in T1512C polymorphism were slightly higher than those with C allele carriers (Hadi Alijanvand et al., [2020](#)). García-Martín et al. ([2018](#)) reported that when certain dose of ethanol were induced, the polymorphism of GABRA6 rs4454083 T/C amongst these individuals were related to motor times, whilst the C/C genotype showed both basal and peak ethanol concentration-faster motor times; this was proposed to be the result of certain subunit expression levels and distribution in human's brain region (García-Martín et al., [2018](#); Rosmond et al., [2002](#); Simpson et al., [2008](#)).

Qiu et al., (2015) reported that hypertension with- or without pre-diabetes increased the chance to suffer from CVDs and T2DM when compared to those with normal blood pressure and blood glucose (Qiu et al., [2015](#)). However, weak associations were observed between blood pressure and genetics and non-genetic factors in the current study. No significant differences of the blood pressure of all participants were observed between different groups of either genetic or non-genetic determinants. Although, we observed significant differences on the FBGs between participants who included and excluded the veggies and fruits in their daily diets. We also found significant correlation between a parameter of physical fitness and the daily intake of veggies and fruits. Healthy eating by consuming the right type and quantity of food from 5 different food groups can ensure the proportional energy produced and prevent the excess calories that may lead to overweight and obesity. Mathur et al., ([2021](#)) reported that motor activity was amongst determinants of non-communicable diseases (NCD) risk factors in 1531 adolescents aged 15-17 years old in India. They observed that insufficient levels of physical activity was found in approximately 6.2% of overweight and 1.8% obese adolescents. A study by Chiriboga et al., ([2008](#)) reported that men gained 0.3 kg whilst women lost 0.2 kg over the 1-year study period. They also observed that greater leisure-time physical activity was amongst predictors for lower body weight at the baseline in both groups. Lower percentage of caloric intake and greater occupational physical activity were reported to correlate with lower body weight in men whilst increased total calorie intake and leisure-time in women were counted for the longitudinal predictors of 1-year weight gain. The study reported that children with overweight and obesity would likely suffer from similar conditions in their future life and increase the risk

of suffering from chronic diseases such as metabolic syndrome and CVDs.

Strength and Limitation

A novel aspect of this study is the investigation of both genetic and non-genetic factors as potential determinants correlated to the cardiovascular diseases risks and neuromuscular fitness. However, due to relatively limited and homogenous sample numbers with a cross-sectional type of study, the metabolism dynamic could not be captured thoroughly; extrapolation of results to other groups must be done in discretion.

Conclusions

Genetic polymorphism of SLC6A4 and GABRA6 along with the daily diets show significant correlations with the fasting blood glucose and the physical fitness levels in these seemingly healthy young adults.

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Conflict of Interest

The authors have declared no conflicts of interest.

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