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ORIGINAL ARTICLE

Triglyceride/HDL-cholesterol ratio and plasminogen activator inhibitor-1 independently predict high pulse pressure in sickle cell trait and disease

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ABSTRACT

We hypothesised that TG/HDL-C ratio and PAI-1 would be associated with high pulse pressure (PP) in young adults with sickle cell trait (SCT) and sickle cell disease (SCD). We compared the clinical, biochemical, and cardiometabolic parameters among individuals with normal genotype (HbAA; $n = 60$), SCT (HbAS; $n = 60$), and SCD (HbSS; $n = 60$), all in steady state. Using multivariate linear regression analysis, high PP was positively related to TG/HDL-C ratio in SCT ($\beta = 0.307$; $p = .014$) and PAI-1 ($\beta = 0.499$; $p = .001$) in SCD. The curve of receiver operating characteristic also showed that TG/HDL-C ratio and PAI-1 are efficient predictors of high PP in SCT carriers and SCD patients, respectively. This study suggests that increased levels of TG/HDL-C ratio and PAI-1 may be salient risk factors that would promote the development of arterial stiffness and other CVD in SCT carriers and SCD patients.

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Introduction

Sickle cell disease (SCD) is a severe inherited disorder of the blood which results from a single point mutation in the gene that codes for the β-globin chains of haemoglobin (Hb), resulting in the polymerisation of red blood cell (RBC) upon deoxygenation (Lozano *et al.* 2012). SCD affects approximately 300,000 live births globally per year, with Nigeria alone accounting for more than 100,000 live births every year. Sickle cell trait (SCT) is a heterozygous form of SCD having about 30–40% of their Hb as the sickle variant, affecting over 200 million people worldwide (Piel *et al.* 2013). SCT is commonly considered to be a relatively benign form of SCD with a normal life expectancy; however, conditions such as dehydration, hyperviscosity, hypoxia, and acidosis could enhance sickling of erythrocytes leading to increased risk of vaso-occlusion (Connes *et al.* 2008). It is now becoming increasingly clear that SCT is also associated with certain adverse outcomes, which include splenic infarction, venous thromboembolism, renal dysfunction, retinopathy, and sudden death (Lemaire *et al.* 2013, Key *et al.* 2015).

Elevated pulse pressure (PP), a surrogate of arterial stiffness (Novelli *et al.* 2014), has of recent emerged to be independently associated with cardiovascular disease (CVD) and is considered to also be a poor prognostic factor in patients with increased risk of CVD (Fernandez-Fresnedo *et al.* 2006). Arterial stiffness, left ventricle ejection fraction and pulse wave velocity (PWV) are the main factors that influence PP. From these hemodynamic factors that influence PP, arterial stiffness and PWV have been documented to independently predict CVD (Safar *et al.* 2013). In SCD patients, literature have reported an increase in PP, and arterial stiffness (Belizna *et al.* 2012) and this increase may cause greater vascular load on the heart, leading to heart failure, myocardial hypertrophy, and end-organ damage (Laurent *et al.* 2009, Benetos *et al.* 2010, Rosano *et al.* 2013). However, published literature on PP in SCT is scarce (Bayramoğlu *et al.* 2013).

The association between atherogenic indices such as triglyceride/high density lipoprotein-cholesterol (TG/HDL-C) ratio and PP has been previously evaluated in individuals with HbAA (Frontini *et al.* 2008). However, this association has not been documented in SCT carriers and SCD patients (Buchowski *et al.* 2007, Zorca *et al.* 2010). In SCD patients, there have been variable reports on lipid profile (Rahimi *et al.* 2006; Buchowski *et al.*, 2007). There is a paucity of information in literature on lipid profile in SCT (Rahimi *et al.* 2006).

Plasminogen activator inhibitor-1 (PAI-1), a marker of atherothrombotic CVD, is a key regulator of fibrinolysis which acts by inhibiting tissue plasminogen activator (tPA). In normal individuals, increased levels of PAI-1 have been shown

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to be associated with insulin resistance (IR), obesity, diabetes mellitus (DM), and CVD (Cesari *et al.* 2010). Evidence has also established a positive link between PAI-1, TC, LDL-C, and TG, suggesting that an elevated PAI-1 level may increase cardiometabolic disease (CMD) risk (Lira *et al.* 2010). Additionally, studies strongly suggest that C-reactive protein (CRP), also a biomarker of systemic pro-inflammation is directly involved in atherosclerosis. Interestingly, CRP stimulates PAI-1 synthesis and may promote CVD via the PAI-1 induction (Devaraj *et al.* 2003). In SCD patients, elevated PAI-1 level has also been reported in steady state which is further elevated during sickle vaso-occlusive crisis (Nsiri *et al.* 1997), predisposing them to devastating complications such as pulmonary hypertension and stroke (Hillery and Panepinto 2004). Moreover, SCD itself is considered to be an inflammatory process (Platt 2000) capable of promoting oxidative stress. However, there is paucity of information on the association between SCT and PAI-1 levels.

Materials and methods

Patients

This study was carried out in the adult outpatient sickle cell clinics of Ladoke Akintola University of Technology (LAUTECH) Teaching Hospital, Ogbomoso, Oyo State, Nigeriaand University of Ilorin Teaching Hospital (UITH), Ilorin, Kwara State, Nigeria between February 2013 and April 2016, and included a total number of 180 young adults; normal (M/F = 36/24, $n = 60$), SCT (M/F = 24/36, $n = 60$), and SCD (M/F = 22/38, $n = 60$) with ages ranging between 18 and 35 years. SCD patients' inclusion criteria includes, individuals whose Hb electrophoresis showed Hb genotype, those who were in steady-state condition defined as the absence of vaso-occlusive crisis, stroke, acute chest syndrome, priapism, and absence of any symptoms of acute illness, at least 8 weeks before participating in the study. Exclusion criteria for SCD patients includes severe anaemia (haematocrit <18%), pregnancy, presence of acquired or congenital heart disease, blood transfusions in the previous 12 weeks, intake of medications that affects blood rheology, excessive intake of alcohol (more than 16 g daily), and tobacco use. The inclusion criteria for SCT patients are individuals who had Hb genotype AS on Hb electrophoresis, while controls are individuals who had Hb genotype AA on Hb electrophoresis. The control and SCT individuals also had the same exclusion criteria similar to SCD, and they were healthy subjects selected from students and hospital workers, as well as members of the local community. All patients were informed about the purpose and process of the study and they all gave their oral and written consent. The study was conducted in accordance with the guidelines set by the Declaration of Helsinki and was approved by the Ethical Review Committees of LAUTECH Teaching Hospital and UITH.

Clinical data

Weight was measured for all participants without shoes using a weighing scale, and body mass index was calculated (BMI = weight/height^2, Kg/m^2). Height, waist circumference (WC), neck circumference (NC), and hip circumference (HC) were measured using a meter tape. Systolic and diastolic BP was measured at rest between 8:00am and 10:00am in the morning using mercury-in-glass sphygmomanometer (Accousson) after three readings and the average determined. PP was calculated as the difference between systolic BP and diastolic BP. Mean arterial pressure (MAP) was also calculated as $^1/_3$ pulse pressure + diastolic BP. Heart rate (HR) was also measured for all the participants.

Biological data

Blood samples of participants were drawn after a 12-h overnight fasting between 8:00am and 10:00am using automated haematological analyzer, Mindray BC-5300 (In-vitro Diagnostics, London, UK), haematological parameters such as Hb and haematocrit (Hct) concentrations, white blood cell (WBC), red blood cell (RBC), and platelet (PLT) counts were determined. Remaining blood samples were centrifuged at 3000 rpm for 15 min, and plasma was stored frozen until when it was used for biochemical assay. Standard enzymatic-colorimetric method with assay kits supplied by Randox laboratory Ltd. (Co. Antrim, UK) was used to determine fasting plasma levels of triglyceride (TG), total cholesterol (TC), and HDL-cholesterol (HDL-C). LDL-cholesterol was estimated with the use of Friedewald's formula (Friedewald *et al.* 1972). Plasma temperature was maintained at 37 °C in a thermostatic incubator before plasma viscosity was determined by adapted capillary viscometry. Plasma viscosity was estimated as the ratio of the flow time for a given volume of plasma to the flow time for the same volume of distilled water (Famodu *et al.* 1998), while blood viscosity was estimated by modified Vand formula (Gordon 1972). Enzyme-linked immunosorbent assay (ELISA) kits were used to measure CRP and PAI-1. IR/Cardiometabolic markers; TyG, the product of TG and fasting glucose, TyG-WC, and TyG-BMI were calculated (Du *et al.* 2014).

Statistical analysis

Results were presented as means ± standard deviation (SD). Analysis of variance (ANOVA) was used for continuous covariates, to compare biological parameters between groups (with Bonferroni *post hoc* test). Pearson correlation analysis was used for correlations. To identify risk factors associated with increased PP, we used a multivariate linear regression and ROC curve analyses. Significance level was defined as $p < .05$. Statistical analysis was done using SPSS (version 16, IBM SPSS Statistics, Chicago, IL).

Results

Patient characteristics

Summarised in Table 1 are the clinical characteristics of the study population. SCT carriers were younger while SCD individuals were age-matched with controls. Weight, height, BMI, NC, WC, and hip were significantly lower in both SCD

Table 1. Clinical characteristics in study subjects.

Parameters	AA	AS	SS	*p* Value[a]	*p* Value[b]
Age (years)	25.9 ± 5.5	21.6 ± 3.0	25.2 ± 6.7	<.001	1.000
Gender (M/F)	36/24	24/36	22/38		
Weight (kg)	64.1 ± 10.1	56.1 ± 8.1	53.3 ± 8.9	<.001	<.001
Height (m)	1.69 ± 0.1	1.64 ± 0.1	1.65 ± 0.1	.003	.006
Neck circumference (cm)	35.3 ± 2.7	32.3 ± 3.7	32.5 ± 2.2	<.001	<.001
Waist circumference (cm)	80.2 ± 8.0	74.7 ± 6.3	76.8 ± 6.9	<.001	.028
Hip circumference (cm)	94.4 ± 7.7	88.0 ± 7.8	89.4 ± 7.4	<.001	.001
Body mass index (kg/m^2)	22.4 ± 2.9	20.8 ± 2.7	19.6 ± 2.7	.006	<.001
Waist/Hip	0.85 ± 0.1	0.85 ± 0.1	0.86 ± 0.1	1.000	1.000
Systolic BP (mmHg)	112.4 ± 10.4	111.3 ± 11.2	106.1 ± 14.4	1.000	.015
Diastolic BP (mmHg)	75.0 ± 9.5	70.9 ± 8.4	61.1 ± 10.6	.059	<.001
Pulse pressure (mmHg)	37.4 ± 11.0	40.4 ± 8.5	45.0 ± 12.5	.392	.001
MAP (mmHg)	87.4 ± 8.3	84.3 ± 8.5	76.1 ± 10.4	.195	<.001
Heart rate (bpm)	67.3 ± 10.3	67.6 ± 9.7	71.4 ± 11.4	1.000	.097
Systolic BP/Height (mmHg/m)	66.5 ± 6.1	67.7 ± 5.5	64.4 ± 8.3	.978	.293
Diastolic BP/Height (mmHg/m)	44.4 ± 5.5	43.1 ± 4.2	37.2 ± 6.6	.640	<.001
Pulse pressure/Height (mmHg/m)	22.1 ± 6.4	24.6 ± 5.0	27.3 ± 7.3	.099	<.001
MAP/Height (mmHg/m)	51.7 ± 4.9	51.3 ± 4.1	46.3 ± 6.3	1.000	<.001

Means ± SD.
AA: HbAA individuals (control); AS: HbAS individuals (sickle cell trait, SCT); SS: HbSS individuals (sickle cell disease, SCD); BP: blood pressure; MAP: mean arterial pressure.
Significant difference ($p < .05$).
[a]Comparison of AA to AS.
[b]Comparison of AA to SS.

Table 2. Haematological and hemorheological profile in study subjects.

Parameters	AA	AS	SS	*p* Value[a]	*p* Value[b]
Red blood cell (10^{12}/l)	4.8 ± 0.7	4.9 ± 0.5	3.2 ± 0.7	1.000	<.001
White blood cell (10^9/l)	4.1 ± 1.1	4.2 ± 1.3	7.6 ± 3.2	1.000	<.001
Platelet (10^9/l)	227.4 ± 7.2	211.7 ± 6.7	330.7 ± 1.8	1.000	<.001
Haemoglobin (g/dl)	130.4 ± 12.5	127.6 ± 14.3	85.9 ± 14.2	.762	<.001
Haematocrit (%)	42.6 ± 4.7	40.5 ± 4.6	26.6 ± 6.1	.081	<.001
Plasma viscosity	1.8 ± 0.2	1.8 ± 0.4	2.1 ± 0.4	1.000	<.001
Blood viscosity	4.4 ± 0.5	4.3 ± 0.7	4.0 ± 1.0	1.000	.015

Means ± SD.
AA: HbAA individuals (control); AS: HbAS individuals (SCT); SS: HbSSindividuals (SCD).
Significant difference ($p < .05$).
[a]Comparison of AA to AS.
[b]Comparison of AA to SS.

Table 3. Fasting glucose and atherogenic lipid profile in study subjects.

Parameters	AA	AS	SS	*p* Value[a]	*p* Value[b]
Fasting glucose (mmol/l)	4.7 ± 1.2	4.0 ± 0.8	4.3 ± 1.5	.002	.166
Triglyceride (mmol/l)	0.9 ± 0.3	1.0 ± 0.5	1.1 ± 0.4	.147	.032
Total cholesterol (mmol/l)	5.3 ± 1.0	5.4 ± 0.7	4.6 ± 1.5	1.000	.003
HDL-cholesterol (mmol/l)	0.8 ± 0.2	1.0 ± 0.4	0.9 ± 0.3	.001	.010
LDL-cholesterol (mmol/l)	4.1 ± 1.0	3.9 ± 0.9	3.2 ± 1.5	.984	<.001
TG/HDL-cholesterol	1.2 ± 0.4	1.2 ± 0.6	1.2 ± 0.5	1.000	1.000
TC/HDL-cholesterol	7.2 ± 2.0	6.3 ± 2.4	5.3 ± 2.1	.049	<.001

Means ± SD.
AA: HbAA individuals (control); AS: HbAS individuals (SCT); SS: HbSS individuals (SCD); TG: triglyceride; TC: total cholesterol; HDL-C: high density lipoprotein- cholesterol; LDL: low density lipoprotein-cholesterol.
Significant difference ($p < .05$).
[a]Comparison of AA to AS.
[b]Comparison of AA to SS.

patients and SCT carriers. However, when NC and WC were adjusted for height, the WC difference initially observed in SCD individuals was lost. For BP parameter in SCD patients, SBP, DBP, and MAP were lower, PP was higher and heart rate was not different from persons with normal Hb; but when SBP, DBP, MAP, and PP were adjusted for the effect of height since BP parameters are known to be affected by height (Xi *et al.* 2014), the lower SBP initially observed was lost. However, mean values for all BP parameter in SCT carriers were comparable to normal individuals even after adjusting for the effect of height on all the BP parameters (Table 1).

Haematologic and hemorheologic parameters in SCT carriers were all comparable with individuals normal Hb. However, blood viscosity, RBC, Hb, and Hct were lower while WBC, platelet count, and plasma viscosity were higher in SCD patients when compared with normal individuals (Table 2).

Fasting glucose was comparable in SCD individuals but lower in SCT carriers when compared with normal individuals (Table 3). For lipid profile, there was an increased TG and HDL-C, decreased TC, LDL-C, and TC/HDL-C and comparable TG/HDL-C in SCD individuals. However, in SCT carriers, all lipid profile parameters measured were comparable to normal individuals (Table 3).

Finally, Table 4 summarises the mean values of inflammatory and CMD markers in the study subjects. CRP in SCD was higher despite being in steady state while no difference was observed in CRP levels between SCT carriers and normal individual. PAI-1 was significantly elevated while no change was seen in TyG index in both SCD individuals and SCT carriers when compared with normal individuals. However, both TyG-BMI and TyG-WC were decreased in SCT carriers probably due to decreased BMI and WC in this subset of individuals, although only TyG-BMI was reduced and TyG-WC was comparable in SCD individuals.

Correlates of pulse pressure in study subjects

We performed a multivariate correlation analysis of PP and multiple clinical, biochemical parameters, and IR markers in the study population using Pearson's correlation (Table 5). PP was positively associated with platelets, WBC, TG, TG/HDL, plasma viscosity, CRP, and PAI-1. However, there was a negative correlation between Hct and PP. A complete list of all multivariate correlations is reported in Table 5.

Table 4. Inflammatory and cardiometabolic disorder markers in study subjects.

Parameters	AA	AS	SS	*p* Value[a]	*p* Value[b]
C-reactive protein (mg/l)	3.2 ± 4.6	4.5 ± 4.9	5.9 ± 7.3	.587	.035
PAI-1 (ng/ml)	13.5 ± 2.7	67.4 ± 8.3	92.8 ± 5.2	<.001	<.001
TyG index	8.0 ± 0.4	7.9 ± 0.5	8.0 ± 0.6	1.000	1.000
TyG-BMI	179.0 ± 25.9	164.6 ± 25.3	157.5 ± 24.0	.006	<.001
TyG-WC	641.8 ± 69.7	591.6 ± 62.7	618.3 ± 79.2	<.001	.208

Means ± SD.
AA: HbAA individuals (control); AS: HbAS individuals (SCT); SS: HbSS individuals (SCD); PAI-1: plasminogen activator inhibitor-1; TyG index: the product of triglycerides and fasting glucose; BMI: body mass index; WC: waist circumference.
Significant difference ($p < .05$).
[a]Comparison of AA to AS.
[b]Comparison of AA to SS.

Table 5. Partial correlation coefficients of pulse pressure (PP) with clinical and biochemical characteristics in in study subjects.

	PP	
	r	*p*
Neck	−0.038	.617
Waist	0.059	.433
Hip	−0.031	.682
BMI	−0.010	.897
Haematocrit	−0.268	<.001
Plasma viscosity	0.229	.002
Blood viscosity	−0.010	.890
Fasting glucose	−0.112	.135
Triglyceride	0.213	.004
Total cholesterol	−0.068	.365
HDL-C	−0.041	.588
LDL-C	−0.087	.248
TG/HDL-C	0.284	<.001
TC/HDL-C	0.040	.596
C-reactive protein	0.224	.003
PAI-1	0.162	.032
TyG index	0.116	.120
TyG-BMI	0.035	.639
TyG-WC	0.119	.110

WBC: white blood cell; BMI: body mass index; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL: low-density lipoprotein cholesterol; PAI-1: plasminogen activator inhibitor-1; TyG index: the product of triglycerides and fasting glucose; *r*: Pearson's correlation.
Significant difference ($p < .05$).

Table 6. Linear regression in the general population (HbAA individuals), sickle cell trait (SCT) population, and sickle cell disease (SCD) population.

	PP in general population[a]			
	Beta	SE	β	*p*
C-reactive protein	0.726	0.163	0.512	<.001
	PP in SCT carriers[b]			
TG/HDL-C	2.196	0.983	0.282	.029
	PP in SCD patients[c]			
PAI-1	0.071	0.019	0.499	.001
TG/HDL-C	6.434	1.908	0.453	.001

β: regression coefficient; TG: triglyceride; HDL-C: high density lipoprotein-cholesterol; PAI-1: plasminogen activator inhibitor-1.
Significant difference ($p < .05$).
[a]Model 1: $R^2 = 0.262$; $p = .001$.
[b]Model 2: $R^2 = 0.079$; $p = .029$.
[c]Model 3: $R^2 = 0.324$; $p = .003$.

Multivariate linear regression

After performing multivariate linear regression, we showed that the strongest independent determinant of PP in SCT carriers was TG/HDL-C, PAI-1 in SCD patients, and CRP in normal individuals (Table 6). Multiple linear regression analysis results are shown in Table 6.

The curve of the receiver operating characteristic (ROC) was also plotted to establish the relevance of each of the factors predicting PP and their area under the curve (AUC) was compared. The results showed that PAI-1 (0.781) in SCD, TG/HDL-C (0.463) in SCT carriers, and CRP (0.405) in normal individuals were the largest AUC respectively and were the most efficient predictor of PP.

Discussion

The major finding of this study was that TG/HDL-C and PAI-1 are independently associated with high PP in young individuals with SCT carrier and SCD respectively. Though PP was not significantly elevated in SCT carriers when compared to normal individuals, multivariate linear regression and the curve of ROC of our data showed that TG/HDL-C was associated with PP in SCT carriers. Using linear regression and the curve of ROC, our results also show an association between increased PAI-1 and PP. To the best of our understanding, this present study was the first to establish that TG/HDL-C is a strong determinant of PP in young adults with SCT independent of other risk factors.

Pulse pressure (PP) is a known independent risk factor for CVD (Lee *et al.* 1999) and also a surrogate of increased arterial stiffness (Pikilidou *et al.* 2015) among young adults with SCD. Though, there was no significant increase in PP of SCT carrier when compared to individuals normal Hb which is in agreement with results from other studies (Bayramoğlu *et al.* 2013); using multivariate linear regression, TG/HDL-C was the strongest determinants of PP in SCT carriers independent of other risk factors. The AUC of ROC curve when plotted also showed that TG/HDL-C was an efficient predictor of PP in SCT carriers. Only few literatures have attempted to study lipid profile levels in SCT carriers (Rahimi *et al.* 2006), and no literature have documented the link between atherogenic lipids and PP in SCT carriers.

In individuals with normal Hb, the role of atherogenic lipids on PP and arterial stiffness has previously been documented (Mitchell *et al.* 2007, Frontini *et al.* 2008). High TG/HDL-C level have both been linked to several cardiovascular and inflammatory diseases (da-Luz *et al.* 2008, Choy and Sattar 2009). Though the role of TG/HDL-C level in the development of CVD has been debated (Goldberg *et al.* 2011), literature suggests that increased TG/HDL-C level may cause

inflammation and oxidative stress, involved in vascular function modulation (Wang *et al.* 2009). Our results, therefore, suggest that though SCT carriers may have a lower risk of arterial stiffness, elevated atherogenic lipids particularly TG/HDL-C could play a role in the development of arterial stiffness in SCT carriers.

PAI-1 has previously been documented to be positively associated with PP, PWV, and arterial stiffness; which suggests that elevated PAI-1 level may contribute in part to arterial stiffening through its link with PP (Nishiwaki *et al.* 2000, Van-Popele *et al.* 2000, Lieb *et al.* 2009). More so, evidences also suggest that PAI-1 inhibits the activity of plasmin and vascular smooth muscle cells migration involved in vascular remodeling, intima-media thickness, and arterial stiffness (Stefansson and Lawrence 1996). Our findings in this study after using multivariate linear regression showed that both TG/HDL-C and PAI-1 were associated with PP in SCD patients; however, further analysis of our data showed that PAI-1 was a stronger determinant of PP in SCD patients which is in line with evidence from other studies that established that PAI-1 was positively associated with high PP (Stefansson and Lawrence 1996, Nishiwaki *et al.* 2000, Van-Popele *et al.* 2000, Lieb *et al.* 2009).

To determine the predictor of PP in individuals with normal Hb, multivariate linear regression and curve of the ROC was also plotted. Unlike in SCD patients and SCT carriers, our results showed that CRP was independently associated to PP which is in agreement with other studies done in apparently healthy individuals (Yasmin *et al.* 2004). In studies focusing on inflammatory biomarkers, it was demonstrated that there was a positive association between CRP, PP, and arterial stiffness partly due to vascular remodeling and increased PWV (Schnabel *et al.* 2008, Lieb *et al.* 2009).

Previous literature have reported that a decreased blood viscosity and increased plasma viscosity increases risk of CVD (Johnson 2005, Lamarre *et al.* 2014). In SCD patients, blood viscosity is typically lower due to low Hct and Hb (Lamarre *et al.* 2014), while plasma viscosity is known to be higher than individuals with normal Hb (Johnson 2005) which is in agreement with the results in our study. Our results, therefore, suggest that rheological parameters may significantly contribute to the elevated PP in SCD patients.

Studies have demonstrated that high fasting plasma glucose (FPG), IR, and DM compromise both structural and functional vascular integrity through many factors which include inflammation and endothelial dysfunction (Temelkova-Kurktschiev *et al.* 2009, Yasuno *et al.* 2010). Other studies documented that prolonged high FPG could lead to elevated PP and arterial stiffness due to endothelial dysfunction and inflammation (Stehouwer *et al.* 2008). Recent investigations also revealed that "metabolically obese individuals with normal weight" (MONW) termed "metabolically abnormal normal weight" or "normal weight obese"; are gradually becoming common (Meigs *et al.* 2006). MONW are characterised by increased adiposity and IR markers with higher vulnerability to CMD (Meigs *et al.* 2006). Our results, however, showed that plasma glucose was lower in only SCT carrier while IR/CMD markers were lower in both SCT carriers and SCD individuals when compared with normal Hb individuals suggesting that SCT carriers and SCD patients are not likely to be abnormally metabolically obese.

In conclusion, our results showed that TG/HDL-C is strongly associated with PP in SCT carriers suggesting that elevated atherogenic lipid levels may be involved in increased PP and subsequent development of arterial stiffness in SCT carriers. However, in SCD patients, PP is closely linked to TG/HDL-C and PAI-1. Also PAI-1 is strongly associated with PP than TG/HDL-C suggesting that both TG/HDL-C and PAI-1 may be an important predictor of CVD risk and hemostasis may modulate arterial stiffness. Finally, elevation of CRP levels in normal individuals can independently predict increased PP and may be an indicator of increased arterial stiffness. Therefore, this study shows TG/HDL-C and PAI-1 as useful screening biomarkers in early discovery of arterial stiffness in SCT carriers and SCD patients.

Disclosure statement

No potential conflict of interest was reported by the authors.

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