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Research Article

Low Density Lipoprotein Subclasses in Patients with Acute Coronary Syndrome, Hypertension and Hypertensive Heart Disease in South Africa

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ABSTRACT

The increase in the development of cardiovascular disease (CVD) has led to more investigations of the pivotal components imperative in the prevention and treatment of CVD. Analysis of lipid parameters with patient history has been crucial in risk classification of patients and monitoring treatment. However, there are patients with acute coronary events with normal lipid parameters and family history, which led to the interest in atherogenic LDL sub-fractions. The objective was to observe the lipid profile and LDL species of patients with hypertension, hypertensive heart disease (HHD) and those with acute coronary syndrome (ACS). Method: Plasma from 92 patients was analysed using gradient gel electrophoresis (GGE), serum was analysed for total cholesterol (TC), LDL-C, HDL-C and triglyceride (TG). A self-administered questionnaire was used to collect demographics and relevant histories. A significantly low HDL-C concentration was observed across all patient groups (HTN $p<0.001$, HHD $p<0.001$, ACS $p<0.001$). Analysis of GGE images revealed that increased TG levels and low HDL-C levels associated with a predominance of LDL phenotype B. It was also observed that LDL-C levels exhibited no precipitating role in the development and progression from LDL phenotype A to I and B. Furthermore, not all patients with ACS had a predominance of LDL phenotype B. Conclusion: High TG levels displayed a causal role in the production of smaller LDL particles. The combination of low HDL-C and elevated TG levels were better indicators than the LDL-C level in association with the atherogenic LDL particles in assessment of CVD risk.

Keywords: *LDL particle size, cardiovascular risk, Hypertension, Hypertensive heart disease, Acute coronary syndrome*

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INTRODUCTION

In the discovery of different LDL subclasses that were identified on the basis their size, density, lipid and apolipoprotein content, this translated to a varying level of risk for ASCVD in individuals. This was documented by Rizzo & Berneis who found small dense LDL (sdLDL) particles identified in patients with uncontrolled diabetes, which associated them with a higher risk for atherosclerotic cardiovascular disease (ASCVD) [Rizzo & Berneis, 2006].

The increased atherogenicity of sdLDL is mostly attributed to its small size, which allows it to easily permeate the arterial [Hirayama & Miida, 2012; Nikolic *et al*., 2013] and its increased susceptibility to oxidation, which is due to its reduced anti-oxidative vitamin carrying capacity, low cholesterol and elevated polyunsaturated fatty acid and apolipoprotein B content [Berneis & Krauss, 2002; Ivanova *et al*., 2017]. In addition, sdLDL has reduced affinity for LDL-receptors, hence it is difficult to clear them from plasma [Sharma & Garg, 2012]. Furthermore, these particles have increased affinity for proteoglycans in the arterial walls. Proteoglycans play a pivotal role in the attachment of sdLDL particles to the arterial wall, hence prolonging their tenancy and in so doing increases its time to be oxidized [Hirayama & Miida, 2012; Sharma & Garg, 2012]. A plasma lipoprotein profile with a predominance of sdLDL particles has been linked with an approximately 3-fold increased risk of CAD. The latter substantiates the notion that sdLDL particles are more atherogenic than the larger and more buoyant LDL particles [Berneis & Krauss, 2002].

A study by Khine & Marais, 2016, at the Dr George Mukhari hospital, in South Africa showed that most of the patients with established myocardial infarction and ASCVD showed normal LDL cholesterol (LDL-C) and HDL cholesterol (HDL-C) levels. However, patients attending the hypertension clinic at this hospital showed progression to

hypertensive heart disease (HHD) and later on developed acute myocardial infarction (AMI) and they account for 45% of patients attending cardiology clinic [Khine & Marais, 2016].
The above highlights the limitations of relying on the standard serum lipid profile measurements as risk factors for coronary artery disease (CAD); hence further risk assessment such as the determination of the LDL subclasses profile in these patients may explain their disease progression. Such investigations have never been done in this population and this study proposes to evaluate the LDL particles in patients with primary hypertension, HHD and those with a history of AMI using the method of polyacrylamide gradient gel electrophoresis (GGE).

MATERIALS AND METHODS

A prospective observational and descriptive study consisting of 129 patients: 60 in the hypertensive group, 47 in the HHD group and 22 in the acute coronary syndrome (ACS) group. Patients were classified as hypertensive if they had a perpetually increased blood pressure hypertension (BP 140/90 mm Hg) or, diagnosed by family physicians or were on antihypertensive medication. HHD patients (presenting with left ventricular hypertrophy, systolic and diastolic dysfunction which manifested clinically as arrhythmias and symptomatic heart failure) were diagnosed by the physicians at the internal medicine outpatient clinic. The ACS group included patients with previously diagnosed AMI, and were recruited from the cardiology clinic. Sixty-one patients with hypertension, 46 patients with HHD, and 21 patients with known ACS who were all on treatment were recruited for this study six weeks after discharge from an AMI attack.

There was no exclusion for age and gender, or comorbidities. Patients with the aforementioned three conditions were randomly selected from the clinic registers. A standard questionnaire was used to collect patient demographics, medical and family history, life style, and medications. Samples from two healthy, normolipidemic normotensive and non-diabetic patients were included to serve as controls. These individuals did not have a personal or family history of heart disease, were not on lipid altering medication and showed lipid profiles within age and gender reference ranges. Ethical approval was obtained from the Sefako Makgatho University Ethics Committee and written consent was given by patients in this study.

Sample collection and laboratory analysis:: From each study participant and control, 3 ml of blood was collected into a serum separation gel tube and another 3 ml into an EDTA plasma tube. After blood collection, serum and plasma were separated from the cells. Serum was used for lipid profiling [total cholesterol (TC), triglycerides (TG), LDL-C and HDL-C], and plasma for lipoprotein sub-classification by GGE. The remaining separated samples were stored at -80°C in case there was a need to perform repeat testing. Laboratory results from lipid profiles were entered into an excel sheet. Non-HDL-C was calculated by subtracting HDL-C from TC., TC, LDL-C, HDL-C and TG were analysed using enzymatic-colorimetric assays on the automated chemistry analyser Architect 8200ci (Abbott, Weisbaden, Germany). LDL-C was directly measured.

GGE technique: LDL particle size was determined using the gradient gel electrophoresis technique as described by Blom *et al*., 2003. Sudan black (50 µl) and saturated sucrose (50 µl) were added into two separate tubes for each plasma sample. Plasma (100 µl) was added to the tubes containing Sudan black, and the mixtures were vortexed. Following this, 50 µl of the plasma/Sudan black mixture was transferred to the tube containing the sucrose and then vortexed. Polyacrylamide gels (2%-8%) were hand-cast and after polymerization the gels were immersed in a tris-glycine buffer (pH 8.3), and each lane of the gel was loaded with 12 µl of the prepared sample. Electrophoresis was carried out at 120 V for 17.5 hours at 4°C using the BioRad Mini-Protean Tetra Electrophoresis System. Gels were scanned and visually analysed using the BioRad Gel Doc EZ Imager (Bio-Rad, Hercules CA, USA).

Statistical analysis: SPSS version 25 (IBM corp, New York) was employed to present patient demographics and descriptive information obtained from the standard questionnaire in the frequency table, with associated p-values for significance. Using Excel ToolpakTM, continuous data (laboratory parameters) that are normally distributed were reported as mean ± SD and those that were of a non-Gaussian distribution were presented as an interquartile range (median, Q1-Q3), then log transformed and compared with age and gender specific reference ranges. A one sample t-test and an ANOVA test was used to compare means or medians, and the chi square test to compare categorical variables. A p-value of less than 0.05 was considered significant.

RESULTS

A standard questionnaire was used to collect the patient demography and associated risk factors such as life style and drug history as important risk factors for ASCVD. The study consisted of a majority of patients that were of advanced age and only seven subjects that were of a younger age (≤ 35 years). Patients were on a high carbohydrates and low protein diet with small amounts of vegetables and fruits. Vegetables were mostly cooked and they were not on vitamin supplements. The demographic and descriptive data is shown in Table 1.

Table 2 presents lipid profiles, non-HDL cholesterol and glycated haemoglobin (HbA1C) variables in their median and IQRs with associated p values in three subgroups of patients. HbA1C was measured for all patients as some patients may be not aware of their status and diabetes is one of the confounding factors for dyslipidaemia.

In GGE analysis, unsuitable plasma samples due to insufficient volumes were excluded from the gel electrophoresis, which left a total of 92 suitable patient samples for analysis. There are 2 control samples (shown as "C") on each gel. Interpretation of LDL phenotypes is shown below the gel picture with the corresponding lane number. Control samples from two healthy individuals showed LDL phenotype A.

Table 1
Patient demographics

		HTN patients (n=60)	HHD patients (n=47)	ACS patients (n=22)	P
	Age (years)	61 (54-71)	66 (57-75)	62 (54-68)	0.353
	Gender (F/M)	40/20 (F=66.6% M=33.4%)	32/15 (F=68.1% M=31.9%)	10/12 (F=45.5% M=54.5%)	0.003*
Co-morbidities:	**Diabetes**	18 (30%)	9 (19.1%)	7 (31.8%)	0.367
	Renal disease	5 (8.3%)	7 (14.9%)	1 (4.5%)	0.342
	Thyroid disease	1 (1.7%)	-	-	-
Life style:	**Smoking**	6 (10%)	3 (6.4%)	3 (13.6%)	0.607
	Alcohol use	26 (43.3%)	12 (25.5%)	5 (22.7%)	0.078
Medication	Simvastatin	13 (21.6%)	19 (40.4%)	17 (77.3%)	<0.001*
	Aspirin	-	18 (38.3%)	20 (90.9%)	<0.001*
	Diuretics	13 (21.7%)	17 (36.2%)	-	0.007*
	Beta blocker	41 (68.3%)	23 (48.9%)	22 (100%)	<0.001*
	ACE inhibitors	28 (41.7%)	14 (29.8%)	20 (90.9%)	<0.001*
	Calcium channel blocker	-	-	20 (90.9%)	-
	Antiplatelet agents (Clopidogrel)	-	-	12 (57%)	-

Table 2:
Lipid profiles of participants in 3 sub-groups

Variable	**Upper limit of normal**	**Hypertensive patients (n=60)**		**HHD patients (n=47)**		**ACS patients (n=22)**	
			P value		**P value**		**P value**
TC (mmol/L)	<5	4.5 (3.6-5.2)	0.012*	4.03 (2.9-4.8)	<0.001*	3.6 (3.1-4.7)	<0.001*
TG (mmol/L)	<1.70	1.3 (0.9-2.1)	0.532	1.3 (0.8-2.2)	<0.001*	1.3 (1.0-1.9)	<0.001*
HDL-C (mmol/L) Females	≥1.2	1.3 (1.0-1.6)	0.033*	0.8 (0.5-1.2)	0.001*	0.8 (0.6-1.3)	0.051
HDL-C (mmol/L) Males	≥1.0	0.9 (0.8-1.3)	0.846	0.7 (0.5-1.1)	0.034*	0.7 (0.7-0.9)	<0.001*
LDL-C (mmol/L)	≤ 2.58	2.8 (1.9-3.3)	0.109	2.2 (1.7-3.1)	<0.001*	2.2 (1.9-2.9)	<0.001*
Non-HDL-C (mmol/L)	<4	3.3 (2.5-3.9)	<0.001*	3.1 (2.1-3.8)	<0.001*	2.8 (2.6-3.8)	<0.001*
HbA1C (%) [DM patients]	<6.5	10.2 (7.8-12.3)	<0.001*	7.9 (6.6-14.6)	<0.001*	8.5 (6.9-9.8)	0.021*

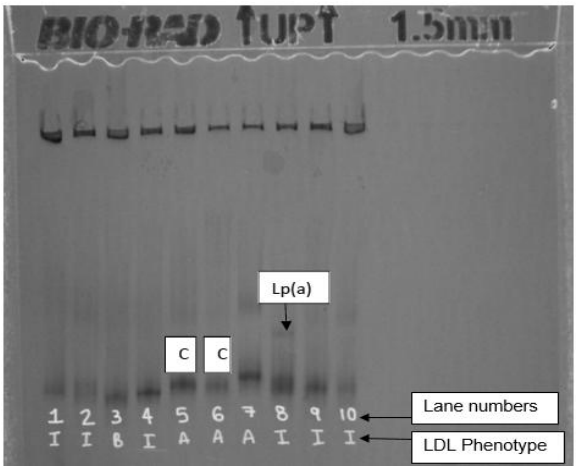

Figure. 1.
LDL phenotypes shown under each gel for a number of patients in correspondence with the lane numbers of the gel. The three major phenotypes namely A (large and buoyant species), I (intermediate species) and B (small and dense species).Lane 8 showing the presence of lipoprotein A [Lp(a)].

LDL phenotypes were presented in 3 subgroups with associated lipid profile, HbA1C (%), age and gender, medication. (Table 3, 4 and 5).

DISCUSSION

LDL particle size carries an element of lipid atherogenicity that is not entirely elucidated by LDL-C levels alone [Ivanova *et al*, 2017], hence this study investigated LDL particle size in three subset groups, which hypertensive patients (n=60), those with HHD (n=47) and patients with known ACS (N=22). From the total number of samples that were analysed using GGE (n=92), large LDL particles (phenotype A) were found to be the predominant species in 55% of the study population, 16% presented with a predominance of sdLDL (phenotype B) and 28% had an intermediate species of LDL (between phenotype A and B).

An interesting finding in this study was that the HDL-C levels of all three groups were much lower than the lower limit of normal see table 2. The use of antihypertensive medication such as thiazides and beta blockers could attribute to this as they have shown to have negative effects on lipids, in particular it has been found that they decrease HDL-C levels. Of note is that the degree of these effects were found to be clinically inconsequential [Deano & Sorrentino, 2012; Marketou *et al*, 2017; Scheen, 2018]. In addition, literature shows that HDL function and size are altered during inflammation, and consequently, a decrease in the cholesterol efflux capacity of HDL occurs along with the loss of its ability to serve as an antioxidant (Hafiane & Genest., 2015; Shrivastava *et al*, 2015; Ramasamy, 2018).

Table 3:
Distribution of diabetes patients, HbA1C values and lipid profiles amongst the different LDL phenotypes in the hypertensive group

LDL pheno-type	N (%)	Gender	Age range Years	TChol (mmol/L)	TG (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L) Females	HDL-C (mmol/L) Males	Non-HDL-C (mmol/L)	DM patients n=18	HbA1C (%) of DM patients
				Ref Interval (<5)	Ref Interval (<1.7)	Ref Interval (<2.58)	Ref Interval (≥1.2)	Ref Interval (≥1.0)	Ref Interval (<4)		
A	27 (61.4)	F=59.3% M=40.7%	59 (44-64.3)	4.6 (3.6-5.2)	1.2 (0.8-1.9)	2.8 (1.8-3.2)	1.5 (1.1-1.6)	1.0 (0.8-1.3)	3.2 (2.3-3.9)	N=11 (61%)	8.0 (6.8-10.4)
I	13 (29.5)	F=67% M=33%	63.5 (52.3-82)	4.4 (3.5-4.6)	1.3 (0.5-2.4)	2.2 (1.8-2.9)	1.2 (1.1-1.9)	0.8 (0.6-1.1)	2.8 (2.1-3.7)	N=6 (33%)	11.5 (10.2-12.4)
B	4 (9.1)	F=100% M=0	68 (49.8-73.5)	4.4 (3.4-5.1)	1.6 (1.1-2.4)	2.4 (1.9-3.2)	1.1 (1.0-1.3)	-	3.2 (2.3-3.9)	N=1 (6%)	14.9

Table 4:
Distribution of diabetes patients, HbA1C values and lipid profiles amongst the different LDL phenotypes in the HHD group

LDL phenotype	N (%)	Age range (years)	Gender	TChol (mmol/L)	TG (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L) Females	HDL-C (mmol/L) Males	Non-HDLC (mmol/L)	DM patients n=9	HbA1C (%) of DM patients
				Ref Interval (<5)	Ref Interval (<1.7)	Ref Interval (<2.58)	Ref Interval (≥1.2)	Ref Interval (≥1.0)	Ref Interval (<4)		
A	19 (57.6)	65 (55.5-75)	F=57.9% M=42.1%	3.9 (2.7-4.8)	1.1 (0.9-2.2)	2.1 (1.7-3.2)	0.8 (0.5-1.0)	0.7 (0.5-1.3)	3.2 (2.2-3.8)	N=5 (56%)	6.6 (6.6-15.0)
I	8 (24.2)	58 (51.3-60.8)	F=75% M=25%	4.1 (3.4-5.1)	1.4 (0.9-2.2)	2.5 (2.0-3.1)	0.7 (0.6-0.9)	0.8 (0.5-1.2)	3.3 (2.6-4.0)	N=1 (11%)	15.0
B	6 (18.2)	70 (67.5-76)	F=33.3% M=66.7%	4.2 (3.5-5.1)	1.7 (1.3-2.4)	2.5 (1.9-3.4)	0.8 (0.5-1.2)	1.0 (0.8-1.1)	3.4 (2.6-3.9)	N=3 (33%)	8.5 (7.9-14.2)

Table 5 :
Distribution of diabetes patients, HbA1C values and lipid profiles amongst the different LDL phenotypes in the ACS group

LDL pheno-type	N (%)	Age range Years	Gender	TChol (mmol/L)	TG (mmol/L)	LDL-C (mmol/L)	HDL-C (mmol/L)	HDL-C (mmol/L) Males	Non-HDLC (mmol/L)	DM patients n=7	HbA1C (%) of DM patients n=7
				Ref Interval (<5)	Ref Interval (<1.7)	Ref Interval (<2.58)	Ref Interval (≥1.2)	Ref Interval (≥1.0)	Ref Interval (<4)		
A	5 (33.3)	64.5 (50.3-78)	F=100% M=0	3.1 (2.8-4.1)	0.8 (0.5-1.7)	2.1 (1.6-2.4)	0.8 (0.3-1.0)	-	2.4 (2.2-3.3)	N=5 (71%)	8.8 (6.9-11.9)
I	5 (33.3)	60 (49-74)	F=60% M=40%	3.6 (2.9-4.5)	0.7 (0.5-1.9)	1.8 (1.4-3.1)	0.8 (0.6-0.8)	1.0 (0.9- 1.0)	2.7 (2.3-3.6)	N=1 (14%)	7.9
B	5 (33.3)	65 (58-72.5)	F=40% M=60%	4.1 (3.1-6.7)	1.2 (0.9-3.2)	2.3 (1.8-4.5)	1.1 (0.6-1.5)	0.7 (0.6-1.1)	2.6 (2.5-5.8)	N=1 (14%)	8.5

This study observed an association between serum TG levels and phenotype B in all three study groups. This phenomenon was explained in literature [Ivanova *et al*., 2017]. When plasma TG levels were normal, the liver secreted primarily apolipoprotein E-containing TG-rich VLDL that was rapidly removed from the circulation. In hypertriglyceridemia, however, the balance was shifted towards apolipoprotein C-III-containing TG-rich lipoproteins that had longer circulation times and were converted into sdLDL. Clearance of apolipoprotein E-containing lipoproteins was also reduced. As a result, a high rate of sdLDL formation and reduced clearance led to the development of phenotype pattern B with elevated sdLDL levels. These observations highlight the importance of controlling hypertriglyceridemia for reduction of CVD risk [Hirayama & Miida, 2012; Ivanova *et al*., 2017]. Hypertriglyceridemia is also associated with low HDL-C levels due to increased transfer of TG from triglyceride-rich lipoproteins such as VLDL, remnant lipoproteins and sdLDL to HDL. This process modifies HDL particles to produce small HDL particles that are small with a core depleted of cholesteryl esters, thus leading to their excretion by the liver and the kidneys. This associates hypertriglyceridemia and phenotype B with a reduced number of HDL particles and the levels of HDL-C [Kwiterovich, 2002; Zeljkovic *et al*., 2008;]. This was also observed in our study across all three patient groups.

Genetic influences on LDL size have also been observed, in particular a single nucleotide polymorphism (SNP) that alters hepatic sortilin synthesis. Sortilin is a sorting receptor that is involved in hepatic VLDL secretion and LDL uptake. Alterations of this receptor results in a 20% increase in sdLDL production and this SNP has been observed in various racial groups with a 30% occurrence rate [Hirayama & Miida, 2012, Ivanova *et al*, 2017] . The effect of lifestyle (high carbohydrate diet with smoking, drinking and lack of physical activity) was also seen in our study to associate with phenotype B of LDL amongst three study groups. Prevalence of phenotype B was also seen with increasing age in this study.

LDL phenotype A was found in 61.4% of patients of the hypertensive group (table 3) which is least atherogenic, although a considerable number of patients (29.5%) were found to have the I phenotype which carry some risk for CVD. There were 9.1% of patients showing the B phenotype (sdLDL) in the hypertensive group with high risk of atherogenicity. Looking closely at the lipid profile parameters, the phenotype B did not associate with TC concentration but it did correspond with increasing values of TG in this study group. Despite having the highest LDL-C values, the patients in this group showed phenotype A, thus LDL-C levels did not correspond with LDL size. Notably, the HDL-C values were lowest in the phenotype B patients, however all phenotypes had HDL-C levels that were lower than the reference limit for both males and females, thus HDL-C levels did not show any relation to the phenotype of LDL. On the other hand, phenotype A seems to present more in younger patients compared to phenotypes I and B. Phenotype A also showed the lowest concentrations of TG which corresponds with buoyant LDL with a smaller TG content. Both A and B phenotypes in this group (one patient each) showed the presence of Lp(a) (figure 1A and 1B), reflecting the presence of the latter as an independent association from the LDL phenotype. Patients with phenotype B with the presence of Lp(a) would have a higher CVD risk.

A similar trend of phenotypes was seen in the HHD group as in the hypertensive group, with the highest distribution for phenotype A, followed by I, and B having the smallest representation (table 4). However, in this group phenotype A was associated with lowest levels of TC, TG and LDL-C but not with high HDL-C levels. On the other hand, phenotype B associated with highest levels of TC and TG, as well as LDL-C, but surprisingly with also the highest level of HDL-C. Phenotype I associated with the lowest levels of HDL-C. Notably again, in this group, the age range of phenotype B was much older (65-76 years, table 4). In this group 5% of patients did not show any predominant LDL phenotype meaning there was an equivalent number of LDL particles spreading across the region of LDL in these patients, thus their CVD risk estimation would not be based on the LDL size. One patient was found to also have Lp(a) and LDL phenotype I adding the risk of atherogenicity synergistically in this patient (figure 1C).

In the ACS group, phenotype I was observed in the majority of patients in this group followed by phenotype A, then phenotype B (table 5). This shows that not all patients with ACS associate with the atherogenic LDL phenotype B. However, their phenotypes showed intermediate atherogenicity inferred by LDL phenotype I. Not surprisingly, the phenotype B did associate with the highest level of TG, but with the lowest levels of LDL-C and high levels of HDL-C implying that serum TG level seems to be a stronger association of LDL phenotype B, which has been observed in this study across all three patient groups. Two patients in the ACS group with LDL phenotype I and B also showed the presence of Lp(a) (figure 2C) which may have contributed in the development of worsened atherogenicity of these phenotypes despite their lower LDL and higher HDL levels. This supports Lp(a) being an independent risk factor for atherosclerosis [Orso & Schmitz, 2017], and this study suggests that it also acts in synergy with atherogenic lipoproteins [Zhao *et al*, 2016].

A trend was observed in the diabetic patients in all three patient groups in which HbA1C values were highest for the LDL phenotype B compared to phenotypes A and I. LDL phenotype B prevails in diabetic patients regardless if the patient has only hypertension or HHD or already has suffered from ACS. In general, prevalence of the phenotype B is approximately 30% in adult men, 5–10% in young men and women (5-20 years), and approximately 15–25% in post-menopausal women [Rizzo & Berneis, 2006; Hirayama & Miida, 2012; Sharma & Garg, 2012].

Five patients (33.3%) in the ACS group showed LDL phenotype A which is thought to be normal type. This suggests that there may be other forms of LDL that are modified to create risk for these patients in developing coronary atherosclerosis such as oxidised LDL, phospholipase A2 enriched LDL particles, desialyted and electronegative LDL,

all of which also pose risks to develop ASCVD [Macphee *et al*., 2005]. Some patients (two in HTN, one in HHD, and two in ACS groups) also showed the presence of Lp(a), showing the advantage of GGE testing in the identification of Lp(a) and LDL typing simultaneously.

Treatment guidelines have stated LDL-C as a primary target to reduce CHD risk [Ramasamy, 2018]. However, regardless of LDL-C lowering, there remains a significant residual risk of CHD in patients receiving LDL-C lowering treatment and in addition, patients with ACS do not always present with increased levels of LDL-C [Khalil *et al*, 2017]. Severe dyslipidaemia as observed in disorders such as familial hypercholesterolemia (FH) are easily indentified in a conventional lipid profile, along with the associated risk CHD risk. In patients with a far less severe lipid profile, the use of LDL-C as a focal point for treatment and risk assessment is a less optimal strategy [Langlois *et al*, 2019]. In light of this a more vigorous approach in risk assessment as well as treatment of CHD may be justified. It has been observed that there is an association between CHD and the predominance of sdLDL, thus evaluation of sdLDL might be helpful in the eleucidation of the residual risk in patients with CAD [Khalil *et al*, 2017; Ramasamy, 2018]

In conclusion, the use of gradient gel electrophoresis in the assessment of atherogenicity in the setting of dyslipidaemia, particularly in that of apolipoprotein B containing lipoproteins is a promising and cost-effective measure that adds value in determining risk in mild as well as severe dyslipidemia. The limitations to this study includes the low number of patients in ACS group and the lack of information for Body Mass Index in patient files

Authors' contribution

All authors contributed in the reviewing of data, its interpretation and the discussion. LH and AAK were responsible for the study design, data analysis and interpretation. LCB and DMT contributed in the interpretation of data and supervision of the study. LH drafted the manuscript and AAK was responsible for the final review of the manuscript content.

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