Nutrition, Metabolism and Cardiovascular Diseases

EVALUATION OF REMNANT CHOLESTEROL LEVELS AND MONOCYTE-TO-HDL-CHOLESTEROL RATIO IN SOUTH ASIAN PATIENTS WITH ACUTE CORONARY SYNDROME.

--Manuscript Draft--

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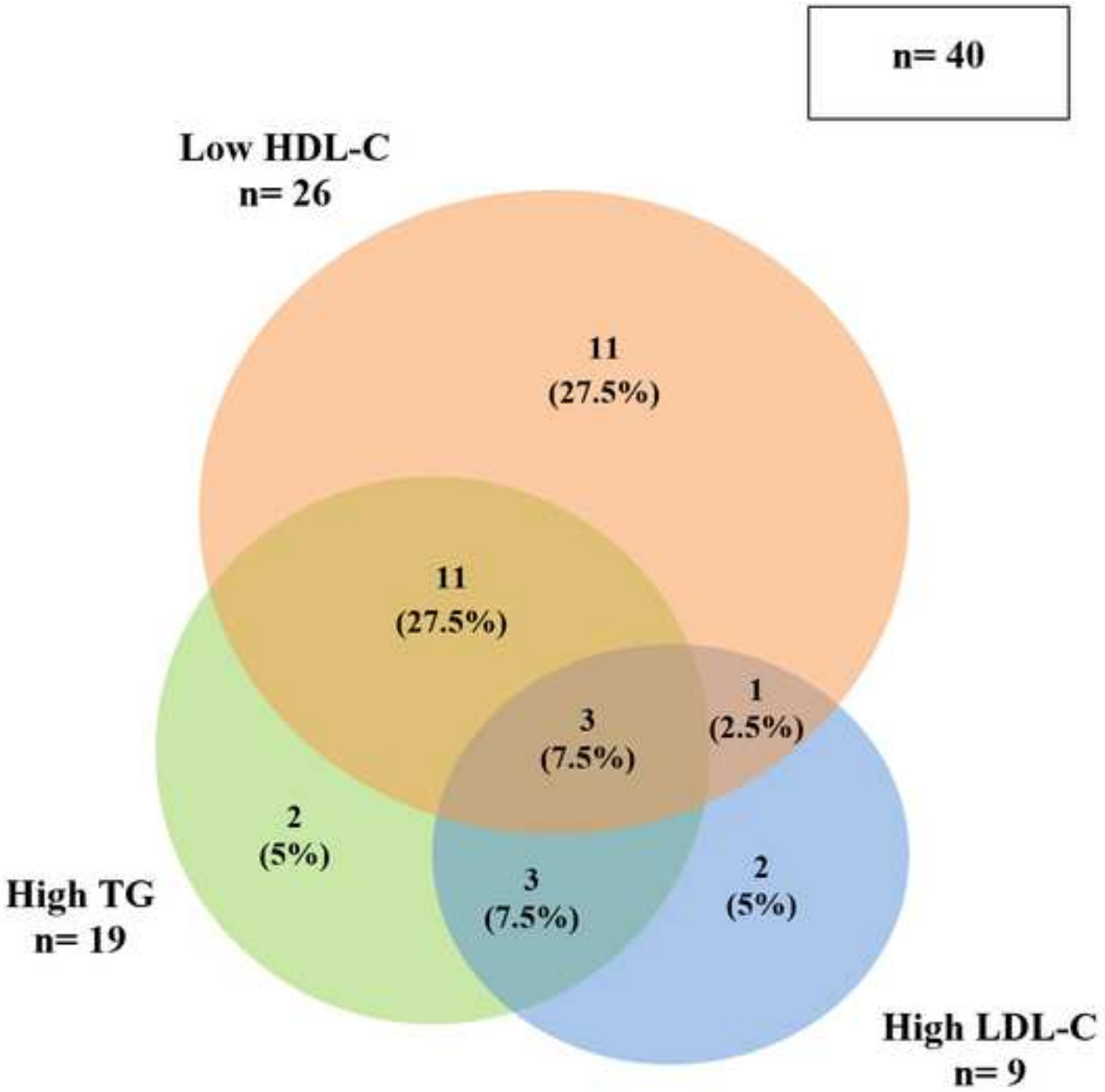
Abstract:	Background and Aims: In the present study, we aimed to compare the clinical and coronary angiography features between South Asian and Caucasian patients with Acute Coronary Syndrome (ACS). In particular, we focused our analysis on the evaluation of recent cardiovascular risk markers, such as remnant cholesterol, corresponding to all plasma cholesterol minus HDL-C and LDL-C, and the Monocyte-to-HDL-cholesterol ratio. We also compared values of several lipoprotein ratios and the Platelet-to-lymphocyte ratio, accurate predictors of coronary events and coronary artery disease. Methods and results: We recruited 40 South Asian and 40 Caucasian patients admitted for ACS. Data were collected by consulting patients' medical records. We used Chi-square test and Student's t-test to analyse qualitative and quantitative variables, respectively. South Asian patients, compared to Caucasians, showed higher mean values of the parameters analysed: remnant cholesterol (32.6 ± 17 vs 26.5 ± 9.6), Monocyte-to-HDL-cholesterol ratio (26.4 ± 48.7 vs 16.5 ± 8.3), Platelet-to-lymphocyte ratio (124.7 ± 130.7 vs 120.5 ± 58.8). Moreover, higher mean values of several lipoprotein ratios were also found in South Asian patients compared to the control group. However, statistical significance was not reached for any of these differences observed. Conclusions: The evaluation of the parameters analysed in this study might provide accurate information regarding the cardio-metabolic risk in South Asian patients. However, further studies with larger samples are needed to obtain more significant results



Figure(s)

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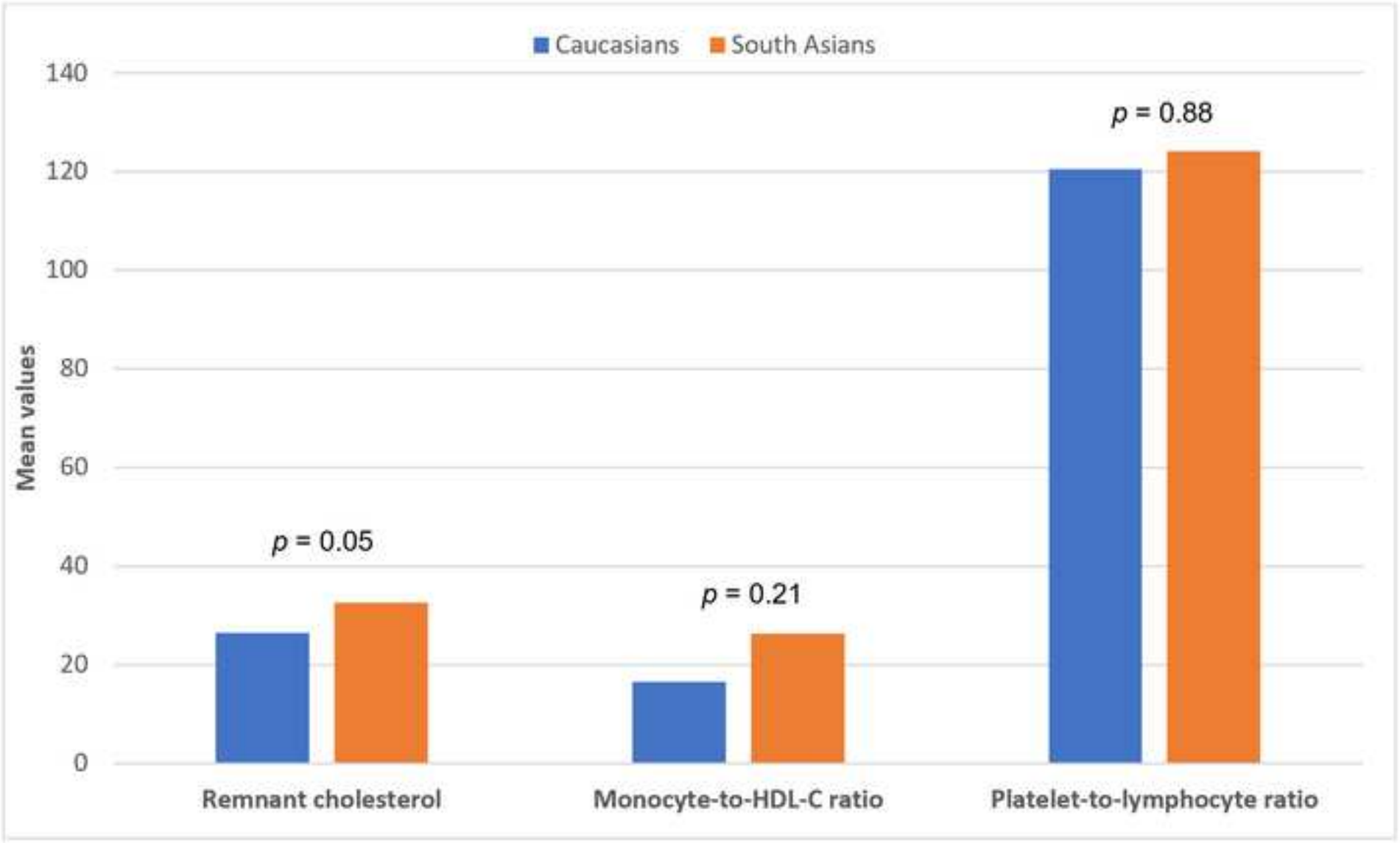

Azienda Ospedaliera Universitaria
Policlinico "Paolo Giaccone" di Palermo

UNIVERSITÀ DEGLI STUDI DI PALERMO

Palermo 15/10/2020

Dear Reviewer,

We would like to submit your attention the manuscript "**Evaluation of remnant cholesterol levels and Monocyte-to-HDL-cholesterol ratio in South Asian patients with acute coronary syndrome.**" This retrospective study allowed us interesting observations about cardiovascular risk in South Asian patients with acute coronary syndrome. Specifically, we focused our attention on two recent cardiovascular risk markers, remnant cholesterol and Monocyte-to-HDL-cholesterol ratio, that have never been assessed in this population, and might be useful as predictors of coronary artery disease and acute coronary events in South Asian patients. Furthermore, we also evaluated several lipoprotein ratios and the Platelet-to-lymphocyte ratio, which are markers of coronary events that might give further information about cardiometabolic risk in South Asian patients.

The paper is not under consideration elsewhere; none of the paper's contents have been previously published. All authors have read and approved the manuscript and they are readily prepared to make all the suggested changes in order to increase the likelihood of publication of their work in the Journal. All authors disclose with any potential conflict of interest with industry for the preparation of this paper.

Looking forward to hearing from You, I remain
Yours Sincerely,

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Highlights

- South Asians patients have a higher prevalence of coronary artery disease
- South Asian patients have higher levels of pro-thrombotic and pro-inflammatory factors
- Several lipoprotein ratios are cardiovascular risk indicators with a greater predictive power

Dear Reviewers,

1) We focused our attention on the South Asian population which is one of the largest migrant population of our country. Several studies have shown that South Asian population has a higher burden of severe coronary artery disease (CAD) and premature onset of acute coronary events than Caucasian population. Therefore, we wondered if the higher prevalence of acute coronary events in South Asian patients is related on two recent cardiovascular risk markers, *remnant cholesterol* (RC) and *Monocyte-to-HDL-cholesterol ratio* (MHR), which have never been studied in this ethnic group. This risk markers, the lipoprotein ratios and *Platelet-to-lymphocyte ratio,* might explain the higher prevalence of CAD in this population.

2) Thanks for clarifying this point. We certainly forgot to highlight the exclusion of patients with thyroid problems. We screened thyroid ormons in all patients at the hospitalitation time.

3) The inpatients informations, such as anagraphic data, risk factors, comorbility, blood tests, drug history and all clinical course, were collected in a digital database. We provide to create two homogeneous groups, taking into account the gender, age and risk factors (smoking, hypertension, diabetes, obesity, hypertrigliceridemia, hypercholesterolemia, metabolic syndrome, familiarity with cardiovascular disease), as shown in Table 1 (we added a proper Table). According to the ESC guidelines, patients who suffered from myocardial ischemia, such as unstable angina, NSTEMI (*Non-ST elevation myocardial infarction*) or STEMI (*ST elevation myocardial infarction),* underwent revascularization procedure through percutaneous coronary intervention (PCI). HDL-C levels < 40 mg/dL in men and < 50 mg/dL in women, LDL-C levels >129 mg/dL, VLDL-C (very low-density cholesterol) levels > 30 mg/dL, tryglicerid (TG) > 150 mg/dL and total cholesterol (CT) > 200 mg/dL, were considered abnormal. LDL-C levels were calculated by Friedewald formula [LDL = CT – (TG/5) – HDL], taking into account that all patients had TG < 400 mg/dL. MHR were derived from the ratio between monocytes count and HDL levels, whereas PLR were calculated by dividing platlet count by lymphocytes blood count. We also assessed the lipoprotein ratios, sush as: CT/HDL-C, LDL/HDL-C, TG/HDL-C, non-HDL cholesterol/HDL-C. The non-HDL cholesterol includes all cholesterol of the atherogenic lipoproteins (LDL, Lp(a), VLDL, IDL, chilomicroni and remnants) and was calculated by subtracting HDL-C levels from CT levels. Finally, VLDL-C was derived by dividing TG levels by 5.

4) Aware of the limits of a retrospective study, we selected the control group by consecutively recruiting 40 italian patients who have been hospitalized in the same years. They were diagnosed with acute coronary syndrome and have undergone revascularization procedure through percutaneous coronary intervention (PCI). According to us, the different distribution of the traditional risk factors might reflects the fact that the pathological burden is not influenced by the lifestyle changes that they could have adopted in Italy.

5) Thanks for highlighting this point. Anyone was born in Italy and were all migrants, living in Italy (we reported it in Method). Of course due to the small sample size and the limits of a retrospective study, we can't extend our result to the entire South Asian population.

6) Furthermore the calculated LDL-C of serum LDL-C by the Friedewald formula contains a contribution from the cholesterol present in Lp(a), which is not considered. Dahlen's formula modifies the Friedwald formula by using lipoprotein in it. Lp(a) is an established cardiovascular risk factor because of the proatherogenic low-density lipoprotein (LDL)-like properties and the prothrombotic plasminogen-like activity of apolipoprotein(a) apo(a). Nonetheless, the hypothesis that lowering Lp(a) could reduce the risk of cardiovascular events still needs to be demonstrated by randomized clinical trials. Due to the lack of data, we couldn't applied Dahlen's formula.

VARIABLES	South Asians (n= 40)	Caucasians (n= 40)	p-value
Sex (M/F)	34/6	34/6	1,000
Age (average ± SD)	49,8 ± 9,7	54,4 ± 9,2	**0,03**
Hypertension n(%)	21 (52,5)	22 (55)	0,82
Diabetes n(%)	18 (45)	9 (22,5)	**0,03**
Obesity n(%)	4 (10)	15 (37,5)	**0,004**
Metabolic Syndrome n(%)	19 (47,5)	14 (35)	0,26
Hypercholesterolemia n(%)	11 (27,5)	12 (30)	0,8
Hypertrygliceridemia n(%)	19 (47,5)	11 (27,5)	0,06
Smoking n(%)	13 (32,5)	33 (82,5)	**< 0,0001**
Familiarity n(%)	6 (15)	23 (57,5)	**< 0,0001**

Table 1.

TABLES

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Table 1.

VARIABLES	South Asians (n= 40)		Caucasians (n= 40)		p-value
	M	SD	M	SD	
TC/HDL-C	5.5 (2.3 – 37.4)	5.4	4.7 (2.4 – 7.9)	1.3	0.38
LDL-C/HDL-C	3.2 (0.9 – 20.2)	3	3 (1 – 5.6)	1.6	0.71
TG/HDL-C	6.4 (1.1 – 81)	12.4	3.5 (1.3 – 8.8)	1.7	0.15
Non-HDL-C/HDL-C	4.5 (1.3 – 36.4)	5.4	3.7 (1.4 – 6.9)	1.3	0.38

Table 2.

VARIABLES	South Asians (n= 40)		Caucasians (n= 40)		p-value
	M	SD	M	SD	
Remnant cholesterol (mg/dL)	32.6 (9 – 81)	17	26.5 (13 – 53)	9.6	0.05
Monocytes ($x10^3/mm^3$)	0.7 (0.2 – 1.6)	0.3	0.6 (0.04 – 1.3)	0.2	0.41
Monocyte-to-HDL-cholesterol ratio	26.4 (3.6 – 320)	48.7	16.5 (0.7 – 51)	8.3	0.21
Platelets ($x10^3/mm^3$)	244.4 (142 – 467)	76	220 (149 – 401)	57.9	0.11
Lymphocytes ($x10^3/mm^3$)	2.6 (0.5 – 8.1)	1.2	2.2 (0.7 – 4.8)	0.9	0.1
Platelet-to-lymphocyte ratio	124.7 (27.3 – 862)	130.7	120.5 (53 – 280)	58.8	0.88

Table 3.

Conflict of interest form

EVALUATION OF REMNANT CHOLESTEROL LEVELS AND MONOCYTE-TO-HDL-CHOLESTEROL RATIO IN SOUTH ASIAN PATIENTS WITH ACUTE CORONARY SYNDROME.

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ABSTRACT

Background and Aims: In the present study, we aimed to compare the clinical and coronary angiography features between South Asian and Caucasian patients with Acute Coronary Syndrome (ACS). In particular, we focused our analysis on the evaluation of recent cardiovascular risk markers, such as remnant cholesterol, corresponding to all plasma cholesterol minus HDL-C (high-density lipoprotein cholesterol) and LDL-C (low-density lipoprotein cholesterol), and the Monocyte-to-HDL-cholesterol ratio. We also compared values of several lipoprotein ratios and the Platelet-to-lymphocyte ratio, accurate predictors of coronary events and coronary artery disease.

Methods and results: We recruited 40 South Asian and 40 Caucasian patients admitted for ACS. Data were collected by consulting patients' medical records. We used Chi-square test and Student's t-test to analyse qualitative and quantitative variables, respectively.

South Asian patients, compared to Caucasians, showed higher mean values of the parameters analysed: remnant cholesterol (32.6 ± 17 vs 26.5 ± 9.6), Monocyte-to-HDL-cholesterol ratio (26.4 ± 48.7 vs 16.5 ± 8.3), Platelet-to-lymphocyte ratio (124.7 ± 130.7 vs 120.5 ± 58.8). Moreover, higher mean values of several lipoprotein ratios were also found in South Asian patients compared to the control group. However, statistical significance was not reached for any of these differences observed.

Conclusions: The evaluation of the parameters analysed in this study might provide accurate information regarding the cardio-metabolic risk in South Asian patients. However, further studies with larger samples are needed to obtain more significant results.

Key words: Plasma Lipids; Asians; Coronary artery disease; Remnant cholesterol; Monocyte-to-HDL-cholesterol ratio; Platelet-to-lymphocyte ratio.

INTRODUCTION

Several studies have shown that South Asian population has a higher burden of severe coronary artery disease (CAD) and premature onset of acute coronary events than Caucasian population[1-3].

We focused our attention on the South Asian population, which is one of the largest migrant population of our country. Traditional cardiovascular risk factors, as obesity, diabetes and unhealthy lifestyle, can only in part explain this higher predisposition[4]. South Asian patients, indeed, show a higher prevalence of emerging risk factors such as higher levels of pro-thrombotic and pro-inflammatory molecules[5-6].

The aim of this study is to better define factors which determine the higher prevalence of acute coronary events in South Asian patients. In particular, we focused our attention on two recent cardiovascular risk markers: *remnant cholesterol* (RC) and *Monocyte-to-HDL-cholesterol ratio* (MHR). Several studies have recognized these two markers as predictors of acute coronary events, severe CAD and major adverse cardiovascular events (MACE)[7-9]. Specifically, remnant cholesterol is all plasma cholesterol that is not LDL-C (low-density lipoprotein cholesterol) or HDL-C (high-density lipoprotein cholesterol), whereas Monocyte-to-HDL-cholesterol ratio is a simple assessment method of inflammatory status[10].

We wondered if these two recent markers that, according to our records, have never been previously studied in South Asian patients, might influence cardiovascular risk in this ethnic group, in order to better understand the reasons behind the higher prevalence of CAD.

Furthermore, for the same reason, we evaluated several *lipoprotein ratios*, which are cardiovascular risk indicators with a greater predictive power than isolated lipoproteins[11]. Finally, we also assessed the *Platelet-to-lymphocyte ratio* (PLR), a marker of coronary events that gives information about pathways of platelet aggregation and inflammation[12].

METHODS

In this retrospective study we recruited 40 South Asian patients with acute coronary syndrome (ACS), hospitalized in the cardiac intensive care unit of the University Hospital Paolo Giaccone in Palermo, from January 2016 to December 2019. Anyone was born in Italy and were all migrants, living in Italy. According to the ESC guidelines, patients who suffered from myocardial ischemia, such as unstable angina, NSTEMI (*Non-ST elevation myocardial infarction*) or STEMI (*ST elevation myocardial infarction),* underwent revascularization procedure through percutaneous coronary intervention (PCI)[13,14]. We also recruited a control group of 40 Caucasian (Italian) patients, who have suffered from acute coronary syndrome and have been hospitalized in the same years. Specifically, patients of

the two groups were of both genders, older than 18 years old and showed critical stenosis (> 70%) at coronary angiography. We did not include in our study patients with missing data, patients undergoing statin therapy, patients with tumour or thyroid problems as these conditions could interfere with plasma lipid levels. The inpatients informations, such as anagraphic data, risk factors, comorbility, blood tests, drug history and all clinical course, had been taken from their medical records and they have been collected in a database. We provide to create two homogeneous groups, taking into account the gender, age and risk factors (smoking, hypertension, diabetes, obesity, hypertrygliceridemia, hypercholesterolemia, metabolic syndrome, familiarity with cardiovascular disease), as shown in Table 1.

HDL-C levels < 40 mg/dL in men and < 50 mg/dL in women, LDL-C levels >129 mg/dL, VLDL-C (very low-density cholesterol) levels > 30 mg/dL, tryglicerid (TG) > 150 mg/dL and total cholesterol (CT) > 200 mg/dL, were considered abnormal. LDL-C levels were calculated by Friedewald formula [LDL = CT – (TG/5) – HDL], taking into account that all patients had TG < 400 mg/dL. MHR were derived from the ratio between monocytes count and HDL levels, whereas PLR were calculated by dividing platlet count by lymphocytes blood count. We also assessed the lipoprotein ratios, sush as: CT/HDL-C, LDL/HDL-C, TG/HDL-C, non-HDL cholesterol/HDL-C. The non-HDL cholesterol includes all cholesterol of the atherogenic lipoproteins (LDL, Lp(a), VLDL, IDL (intermediate-density lipoprotein, chylomicron and remnants) and was calculated by subtracting HDL-C levels from CT levels. Finally, VLDL-C was derived by dividing TG levels by 5.

As regards the evaluation of RC levels, since they have been analysed through blood samples taken at the moment of patients' hospitalization, we evaluated *non-fasting* RC levels. However, fasting and post-prandial RC levels show little difference, so it is possible to accurately evaluate RC values even in a non-fasting plasma sample.

Data have been analysed through MedCalc programm. We used Chi-square test and Student's t-test to analyse qualitative and quantitative variables, respectively. $p < 0.05$ was set as the level of significance for each test.

RESULTS

South Asian patients group included 34 men (85%) and 6 women (15%) aged 49.8 ± 9.7 years. Specifically, 33 patients (82.5%) were from Bangladesh, 5 (12.5%) from Sri Lanka, 1 (2.5%) from India and 1 (2.5%) from Pakistan. Caucasian patients were all Italian, including 34 men (85%) and 6 women (15%), aged 54.4 ± 9.2 years.

As regards the prevalence of cardiovascular risk factors, South Asian patients showed a higher prevalence of diabetes (45% vs 22.5%, $p = 0.03$), metabolic syndrome (47.5% vs 35%, $p = 0.26$) and

hypertriglyceridemia (47.5% vs 27.5%, p = 0.06) than Caucasians. However, they showed a lower prevalence of arterial hypertension (52.5% vs 55%, p = 0.82), obesity (10% vs 37.5%, p = 0.004), hypercholesterolemia (27.5% vs 30%, p = 0.8), smoking habit (32.5% vs 82.5%, p < 0.0001) and family history for cardiovascular diseases (15% vs 57.5%, p < 0.0001) than the control group.

As regards lipid profile distribution, South Asian patients had higher levels of triglycerides (161.3 ± 85.2 vs 132.4 ± 48.2 mg/dL, p = 0.07) and VLDL-C (32.3 ± 17 vs 26.5 ± 9.6 mg/dL, p = 0.07), but lower values of total cholesterol (170 ± 46.6 vs 181.1 ± 36.7 mg/dL, p = 0.24), HDL-C (37 ± 10.1 vs 40 ± 8.2 mg/dL, p = 0.14), LDL-C (100.4 ± 40.2 vs 114.6 ± 34.3 mg/dL, p = 0.09) and non-HDL-C cholesterol (133.1 ± 45.7 vs 141.1 ± 38.1 mg/dL, p = 0.4) than Caucasians.

In Figure 1, it has been shown the prevalence of isolated- and mixed-dyslipidemias in South Asian patients. We may observe that 26 patients (65%) had low HDL-C values, 19 (47.5%) had hypertriglyceridemia and 9 (22.5%) had high LDL-C levels. To be more specific, 11 patients (27.5%) had isolated values of low HDL-C, 2 (5%) showed an exclusive increase of triglycerides, whereas 2 (5%) simply showed altered LDL-C levels. In addition, 11 patients (27.5%) had both HDL-C and triglycerides abnormal values, 3 (7.5%) showed an increase of both triglycerides and LDL-C levels, whereas only 1 patient (2.5%) showed at the same time low HDL-C and high LDL-C values. Finally, 3 patients (7.5%) showed a coexistence of altered levels in all the three lipidic fractions taken into account.

Afterwards, we estimated various lipoprotein ratios and the results have been represented in Table 2. Mean values of all lipoprotein ratios resulted to be higher in South Asian patients than in Caucasians, although none of these differences reached the statistical significance: TC/HDL-C (5.5 ± 5.4 vs 4.7 ± 1.3, p = 0.38), LDL-C/HDL-C (3.2 ± 3 vs 3 ± 1.6, p = 0.71), TG/HDL-C (6.4 ± 12.4 vs 3.5 ± 1.7, p = 0.15) non-HDL-C/HDL-C (4.5 ± 5.4 vs 3.7 ± 1.3, p = 0.38).

Subsequently, we estimated RC values and MHR and PLR. As we may see in Table 3 and in Figure 2, South Asian patients showed higher values of RC (32.6 ± 17 vs 26.5 ± 9.6 mg/dL, p = 0.05), MHR (26.4 ± 48.7 vs 16.5 ± 8.3, p = 0.21) and PLR (124.7 ± 130.7 vs 120.5 ± 58.8, p = 0.88) than Caucasians. Furthermore, mean values of monocytes, lymphocytes and platelets counts, resulted to be higher in South Asians. However, none of these differences reached statistical significance.

Finally, we compared coronary angiography features in both the two groups, in order to analyse potential differences in their critical stenosis (> 70%) distribution. South Asian patients showed a higher prevalence of multi-vessel CAD (15% three-vessel disease and 35% two-vessel disease) than Caucasian patients (0% three-vessel disease and 2,5% two-vessel disease) and they also showed a higher prevalence of critical stenosis in every examined coronary vessel, which is expression of a more severe CAD: right coronary artery (45% vs 22.5%), left anterior descending artery (57.5% vs 50%), left circumflex artery (57.5% vs 30%), left main coronary artery (10% vs 0%).

DISCUSSION

This study allowed us interesting observations about cardiovascular risk in South Asian patients with acute coronary syndrome. Specifically, we focused our attention on two recent cardiovascular risk markers, remnant cholesterol and Monocyte-to-HDL-cholesterol ratio, that have never been analysed in this population. The first interesting element emerged in our analysis is related to the distribution of lipid profiles. We noticed that South Asian patients had a higher prevalence of isolated low HDL-C levels (27.5%), thus, with no other lipoprotein alterations, but also a higher prevalence of both high triglycerides and low HDL-C levels (27.5%). Conversely, they showed a lower prevalence of isolated abnormal triglycerides (5%) and LDL-C values (5%) or mixed dyslipidemias defined as elevation in LDL-C levels accompanied by low levels of HDL-C (2.5%). As we know, low HDL-C values represent an independent risk factor for CAD, as they cause the lack of the antioxidant function carried out by these lipoproteins, which is related to cholesterol deposit removal from vessel walls and to the reduction of macrophage accumulation in the arterial intima. At the basis of this altered lipoprotein profile, an important role seems to be played by insulin-resistance and by the raising CETP (cholesteryl ester transfer protein) activity that facilitates the transport of cholesterol esters from HDL-C to VLDL-C and LDL-C, resulting in the reduction of HDL-C levels and in the increase of triglycerides[15].

Starting from single lipoprotein values, we decided to estimate different lipoprotein ratios, as they represent cardiovascular risk indicators with a greater predictive power than isolated lipoproteins[11]. TC/HDL-C ratio, known as *atherogenic index*, and LDL-C/HDL-C ratio, seem to have a similar validity, as at least two-thirds of plasma cholesterol resides in LDL-C particles. It has been observed that values of TC/HDL-C ≥ 5.5 and LDL-C/HDL-C > 5 are associated to an increased risk of coronary events[16,17]. In our study, South Asian patients showed higher mean values of these two ratios than Caucasians. In particular, the mean value of TC/HDL-C ratio in South Asian patients is 5.5 ± 5.4, thus, equal to the cut-off value indicative of an increased cardiovascular risk. As regards TG/HDL-C ratio, Da Luz PL. et al.[18] demonstrated that this index is highly related to the extension and severity of coronary lesions, a relationship that resulted to be higher than single lipoprotein values. Furthermore, a TG/HDL ratio > 4 is an important independent predictor for CAD[18]. In our study, South Asian patients showed mean values of this ratio equal to 6.4 ± 12.4, whereas Caucasians had 3.5 ± 1.7. Finally, we analysed the non-HDL-C/HDL-C ratio. We considered this index because non-HDL-C cholesterol, which includes LDL-C, Lp(a), VLDL-C, IDL-C, chylomicrons and their remnants, has been recommended as a secondary therapeutic target in patients with elevated triglycerides and suggested as a possible surrogate marker for apoB concentration. Furthermore, non-

HDL-C/HDL-C ratio seems to have a predictive power for cardiovascular diseases similar to that of TC/HDL-C and LDL-C/HDL-C ratios[19].

Non-HDL-C values > 130 mg/dL are associated with an increased cardiovascular risk and in our study, we detected higher mean values than this cut-off both in South Asian and in Caucasian patients (133.1 ± 45.7 vs 141.1 ± 38.1, respectively).

In addition, South Asian patients showed higher mean values of non-HDL-C/HDL-C ratio than the control group (4.5 ± 5.4 vs 3.7 ± 1.3).

The evidence of higher mean values of all lipoprotein ratios in South Asian patients, compared to Caucasians, may be the consequence of the higher severity of CAD in this ethnic group. However, none of the differences found in these lipoprotein ratios reached statistical significance.

Furthermore the calculated LDL-C of serum LDL-C by the Friedewald formula contains a contribution from the cholesterol present in Lp(a), which is not considered. Dahlen's formula modifies the Friedwald formula by using lipoprotein in it. Lp(a) is an established cardiovascular risk factor because of the proatherogenic low-density lipoprotein (LDL)-like properties and the prothrombotic plasminogen-like activity of apolipoprotein(a) apo(a)[20]. Nonetheless, the hypothesis that lowering Lp(a) could reduce the risk of cardiovascular events still needs to be demonstrated by randomized clinical trials. Due to the lack of data, we couldn't applied Dahlen's formula.

Carrying on our analysis, we estimated RC and MHR, the two cardiovascular risk markers which represent the leading point of our analysis. RC corresponds to all plasma cholesterol minus HDL-C and LDL-C. The idea to estimate this marker in South Asian patients came from the several studies in literature that show how high RC levels determine a higher cardiovascular risk in the general population, as well as a persistent remnant risk of coronary artery events in patients in treatment with statins and with LDL-C values under control[21,22].

Different studies have shown that the progressive increase in non-fasting RC values was significantly related to a higher risk of CAD, acute coronary events and all-cause mortality.

Furthermore, it has been observed that patients with non-fasting RC > 43 mg/dL had a 2-3 times higher risk of ischemic heart disease than patients with non-fasting RC < 15 mg/dL[7,8].

In addition, RC levels in patients with CAD were significantly related both to MACE and to a higher risk of intra-stent restenosis in patients who underwent PCI[23,24].

In our study, South Asian patients had higher mean values of non-fasting RC than Caucasians (32.6 ± 17 vs 26.5 ± 9.6). This result may help us to understand the reasons of the different cardiovascular risk in these two ethnic groups. High RC levels may determine increasing coronary endothelial dysfunction, as RC is made of very small molecules that easily penetrate the arterial wall and

accumulate in the intimal layer determining an inflammatory process that will lead to the formation of atherosclerotic plaques.

Increasing RC levels in South Asian patients may be caused by their unhealthy lifestyle, strongly related to physical inactivity and to a diet low in protein and omega-3 fatty acids and high in total fat and monounsaturated fatty acids.

Additionally, insulin-resistance, which is common in South Asian patients, might have an important role in lipid homeostasis alteration, with increasing circulating pro-atherogenic lipids, including RC. Lifestyle changes, by increasing physical activity or by adopting a Mediterranean-style diet, for instance, might improve lipid profile in this ethnic group. However, in our study, differences observed in RC levels did not result to be statistically significant ($p = 0.05$).

As regards the evaluation of MHR, we observed higher mean values of this ratio in South Asian patients than in Caucasians (26.4 ± 48.7 vs 16.5 ± 8.3), although this difference did not result to be statistically significant ($p = 0.21$). This ratio is an easily calculable recent prognostic cardiovascular marker that gives information about the entity of the inflammation and oxidative stress[9]. The idea to evaluate this index in our study came from the evidence of higher pro-inflammatory adipokines and C-reactive protein (CRP) levels, combined with lower HDL-C values, in South Asian population than in Caucasians[25].

Consequently, the evaluation of MHR might be useful as a predictor of CAD and acute coronary events in South Asian patients. Indeed, this ratio allows the evaluation of two phenotypic traits in South Asian population which are related to a higher cardiovascular risk: systemic inflammation, calculated through the monocytes count, and low HDL-C levels, which determine an increased oxidative stress.

Furthermore, in literature, several studies have shown how this marker may be useful in cardiovascular risk prediction. Korkmaz A et al.[26] identified a MHR cut-off value of 12.1 for prediction of hemodynamically significant coronary artery stenosis in patients who underwent coronary angiography to evaluate fractional flow reserve[26].

In accordance to this, in our study, both South Asian and Caucasian patients had critical coronary artery stenosis and showed mean MHR values higher than 12.1.

Açıkgöz SK et al.[27] demonstrated that MHR is an independent predictor for intra-hospital and long-term mortality and MACE in patients with STEMI. In addition, they found that none of these clinical outcomes was associated to the monocytes count or HDL-C levels, when individually considered[27].

Furthermore, this ratio seems to be independently related to the presence of metabolic syndrome[28]. This evidence might be the explanation for the higher MHR values we found in South Asian patients, who showed also a higher prevalence of metabolic syndrome.

Finally, we assessed PLR. Although, even in this case, the differences found among the two groups

were not statistically significant (p = 0.88), South Asian patients showed higher mean values of this ratio than Caucasians (124.7 ± 130.7 vs 120.5 ± 58.8).

We wanted to analyse even this index, as it gives information about pathways of platelet aggregation and inflammation and it might be more valid for the prediction of cardiovascular risk and coronary damage than platelets and lymphocytes count singularly considered[12].

Indeed, Zhou et al.[29] observed that a group of Chinese patients with STEMI and PLR > 171, showed more severe coronary artery stenosis and a worse prognosis, as well as higher incidence of MACE during a 5 years follow-up, than patients with lower values of this ratio[29].

CONCLUSION

In our study, we observed higher values of remnant cholesterol and Monocyte-to-HDL-cholesterol ratio in a group of South Asian patients compared to a control group of Caucasian patients. In addition, South Asian patients showed also higher values of lipoprotein ratios and Platelet-to-lymphocyte ratio. However, none of these differences resulted to be statistically significant. A routinely evaluation of the parameters analysed in this study, might give further information about cardiometabolic risk in South Asian patients and might be useful to elaborate prevention procedures or pharmacological treatments in order to prevent or reduce CAD extension. However, further studies with larger samples are needed in order to validate the evaluation of these parameters in clinical practice.

LIMITATIONS OF THE STUDY

The main limitation of this study is the too small sample size. Many patients could not be included as they did not respect inclusion criteria, mainly due to the lack of important data to conduct our study.

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LEGEND

Tables:

Table 1. Comparison of lipoprotein ratios between South Asian and Caucasian patients. M: mean values (the minimum and maximum value of the series in brackets); SD: standard deviation; TC: total cholesterol; TG: triglycerides; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol.

Table 2. Comparison of remnant cholesterol, Monocyte-to-HDL-cholesterol ratio and Platelet-to-lymphocyte ratio between South Asian and Caucasian patients.
M: mean values (the minimum and maximum value of the series in brackets); SD: standard deviation.

Figures:

Figure 1. Prevalence of isolated- and mixed-dyslipidemias in South Asian patients. Venn-Diagram displays overlaps between prevalence of high LDL-C, TG and low HDL-C levels in South Asian patients. TC: total cholesterol; TG: triglycerides; LDL-C: low-density lipoprotein cholesterol; HDL-C: high-density lipoprotein cholesterol.

Figure 2. Distribution of remnant cholesterol, Monocyte-to-HDL-cholesterol ratio and Platelet-to-lymphocyte ratio in the two populations of the study.