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Research Article

Disparity of risk factors and concordance of NLR with Gensini score in acute coronary syndrome in an Afro-Arab multiethnic nation

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Abstract

Background: Acute coronary syndrome (ACS), is ischemic heart disease of varying risk factors and clinical pattern and with immense health burden worldwide. Inflammation is believed to be an etiological factor in ACS, and neutrophil to lymphocyte ratio (NLR), to be a biomarker.

Objectives: To describe the clinical pattern and risk factors of ACS in Afro-Arabs of Sudan and to evaluate the NLR as a severity marker.

Method: In a total population, cross-sectional study, conducted in Al-Shaab Hospital- Sudan, clinical, laboratory and ECG data were used for ACS grouping into unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI) and STEMI. All patients underwent coronary angiography (CAG) and their Gensini score and NLR were calculated.

Results: A total of 130 patients (62.3% men) of a median age of 58.0, 50.0-65.0 yrs., (range 32.0-82.0), were diagnosed with ACS; 44.6% STEMI, 37.7% NSTEMI and 17.7% UA. The median Gensini score was higher in STEMI (42.5, 12.0-71.0) and NSTEMI (40.0, 15.8-60.5) compared with UA (10.0, 5.0-23.0), p 0.002, similarly, was the NLR; 3.5, 1.6-4.6; 2.9, 1.5-3.8 and 0.9, 0.8-1.1, respectively $p<0.001$. Furthermore, the NLR in concordance with CAG findings $p<0.001$. Finally, hypertension, diabetes mellitus and dyslipidemia, respectively, were stronger ACS risk factors in women than in men unlike smoking, and family history imposed the least risk.

Conclusion: While the ACS clinical pattern was in-line with literature, the risk factors order was different, and it was different between sexes**.** Importantly, the NLR strongly associated with ACS severity, but failed to distinguish between NSTEMI and STEMI.

Keywords: ACS; ECG; angiography; gensini score; NLR

Abbreviations

ACS	Acute coronary syndrome
MI	Myocardial infarction
CAD	Coronary artery disease
CAG	Coronary angiography
CVD	Cardiovascular disease
DM	Diabetes mellitus

HDL	High density lipoprotein
HTN	Hypertension
LDL	Low density lipoprotein
NLR	Neutrohil lymphocyte ratio
NSTEMI	Non-ST-segment elevation myocardial infarction
STEMI	ST-segment elevation myocardial infarction
UA	Unstable angina

Introduction

Cardiovascular diseases (CVD) are one of the major causes of death worldwide. The World Health Organization declared that CVD are responsible of about 17.9 million death/year, which was 31% of the world deaths in 2016, of which 7.5 million are due to ischemic heart disease (IHD), mainly acute coronary syndrome (ACS) and sudden death [1]. The incidence of IHD increases with age, and it is responsible for more than half of all CVD in the ages < 75 years [2], although this occurs 7–10 years earlier in men compared to women. While the ACS is far more often in men below 60 years, women are the majority over 75 years of age [3].

The ACS refers to a spectrum of clinical presentation ranging from ST-segment elevation myocardial infarction (STEMI) to non–STEMI (NSTEMI) and unstable angina (UA) according to the presence or absence of ST-segment elevation on initial ECG, in addition to measurement of myocardial biomarkers, such as troponin or creatine kinase, however in both condition there is myocardial necrosis [4, 5]. The UA is different from stable angina, which develops during physical activity or stress and resolves at rest, still there is no myocardial necrosis in UA [4, 6].

For ACS patients, coronary angiography (CAG) is usually conducted and assessed by specialized cardiologists. Significant CAD is assumed as a lumen diameter stenosis of ≥50% in the major coronary arteries e.g. left main, anterior descending or circumflex artery coronary arteries, right coronary artery, or one of their major branches [7].

The IHD is caused by atherosclerosis of the coronary arteries, which leads to development of unstable plaque as a result of chronic inflammatory mechanism [8, 9]. The rupture of the plaque is accompanied by a cascade of platelet reactions culminating in formation of thrombus, followed by occlusion of the affected coronary artery then ischemia/necrosis of the underlying myocardial tissue, leading to ACS [9]. Thus, inflammation plays is an important factor in both initiation and progression of atherosclerotic process [10], and increased neutrophil count is known to be associated with the development and severity of coronary atherosclerosis [11]. Neutrophil to lymphocyte ratio (NLR), is a combination of inflammatory markers in which the neutrophils are nonspecific markers of inflammation and lymphocytes are regulatory cells [12]. The association between NLR and various CVD, is well documented, thus there is propensity of the former to evolve into an accurate, inexpensive, and independent prognostic marker for diagnosis of ACS and predictor for its short and long-term mortalities [13]. In a recent study, NLR was found to be associated with severity and plaque morphology in patients with CHD [14], and the high NLR compared to low NLR at admission was found to be associated with higher mortality in STEMI and NSTEMI patients [15]. Furthermore, the NLR is significantly elevated in patients with low HDL-cholesterol and negatively correlated with high-density lipoprotein (HDL) which has anti-inflammatory activity [16]. However, which NLR value is correlated with a higher risk for developing atherosclerosis, which cut-off value will differentiate normal from abnormal results are still debatable. Different values of NLR, with different methods, in different populations are cited, with no universal value is currently available [17].

There is an extreme need for a reliable, accessible, less invasive prognostic marker in ACS that would help in early identifications of patients with high cardiovascular risk. The goal of this study is to describe the ACS risk factors and clinical spectrum in the biggest cardiology center in Sudan and included subjects with different ethnic decent (Afro-Arabs) to evaluate the potential use of NLR as a quick, reliable and affordable biomarker for grading the ACS severity in a country with limited resources. Moreover, the NLR have racial differences, thus it's a necessity that data to be collated from all over the world.

Materials and methods

Study design: Total-population, cross-sectional hospital-based study.

Study area. The study was conducted in Alshaab Teaching Hospital (ATH) in Khartoum, the main cardiac center in Sudan.

Study population: All patients with ACS admitted to ATH in the period from September to December 2020, with confirmed ACS and underwent coronary angiography, were included while active inflammation, infection, malignancy, hematological disorder, autoimmune disease, and immunosuppressive treatments, were the exclusion criteria. The patients were derived from different ethnic backgrounds of varying degrees of African and Arab race crossing.

Data collection: The personal, demographic, clinical and laboratory investigation data were collected from each participant with inclusion of information about potential cardiovascular risk factors e.g. hypertension (HTN), diabetes mellitus (DM), smoking history, dyslipidemia and family history of CAD.

Blood test: Hemoglobin (Hb), total and differential white blood cells (WBC), and platelets count were done using Sysmex XP 300 machine

Neutrophil / lymphocytes Ratios (NLR): The absolute neutrophil count was divided by the absolute lymphocyte count to calculate the NLR.

The ACS diagnosis:

The following investigations were done to patients on arrival in the emergency room **i.** Electrocardiogram (ECG); the resting 12-lead ECG, ii. Cardiac biomarkers: measurement of cardiac troponin (cTn) T or I.

iii. Coronary angiography was done by expert interventional cardiologists.

Based on the clinical data in addition to the cardiac markers and ECG, patient were grouped into, STEMI, NSTEMI and UA [4]. The STEMI is suspected in patients presented with a consistent clinical history and ECG showed persistent (>20 minutes) ST-segment elevation (measured at the J-point) in at least two contiguous leads of ≥ 2.5mm in men < 40 years, ≥ 2mm in men ≥ 40 years, or ≥ 1.5mm in women in leads V2–V3 and/or ≥ 1mm in the other leads, or new left bundle branch block, with elevated cardiac biomarkers. Patients with NSTEMI presented with acute chest discomfort but no persistent ST-segment elevation, there may be other ECG changes or normal ECG. The UA patients were presented chest pain at rest or on minimal exertion associated with ST-segment depression and T-wave inversion, or normal ECG.

Assessment of coronary angiography

Coronary angiography (CAG) was conducted and assessed by experienced specialized cardiologists. Significant vessel disease (stenosis) was defined as a lumen diameter narrowing of ≥50% in the major coronary arteries; left main coronary artery, left anterior descending artery, left circumflex artery, right coronary artery, or one of their major branches. The CAD results categorized as; one-vessel disease

(1-VD), two-vessel disease (2-VD; or left main trunk disease without right coronary artery stenosis) or three-vessel disease (3-VD; or left main trunk disease with right coronary artery stenosis).

Gensini score: Calculation of the Gensini score was initiated by giving a severity score to each coronary stenosis as follows: It defined narrowing of the lumen of the coronary arteries as 1 for 1 to 25% stenosis, 2 for 26 to 50%, 4 for 51 to 75%, 8 for 76 to 90%, 16 for 91 to 99%, and 32 for total occlusion. The score was then multiplied by a factor representing the importance of the lesion location in the coronary artery system. For the location scores, 5 points were given for a left main lesion; 2.5 for the proximal left anterior descending (LAD) or left circumflex (LCX) artery; 1.5 for the mid-segment LAD and LCX; 1 for the distal segment of the LAD and LCX, first diagonal branch, first obtuse marginal branch, right coronary artery, posterior descending artery, and intermediate artery; and 0.5 for the second diagonal and second obtuse marginal branches [18]. Finally, Gensini score of >25 was used to draw a cutoff point for the NLR atherogenic risk, using Receiver Operating Characteristics (ROC) program.

Ethical consideration

Ethical clearance was obtained from the research ethics committee at Sudan medical specialization board. Permission was obtained from A-Shaab Hospital management staff as a site for the study. Written and verbal consents were obtained from study participants. Confidentiality and anonymity of individual identity is maintained.

Statistical analysis

Sigma-Stat software was used for statistical analysis. T-test and One Way of Analysis of variance (ANOVA) were used for comparisons of normally distributed data (mean ± SD), while Mann-Whitney Rank Sum Test (MW) and Kruskal-Wallis One Way Analysis of Variance on Ranks (KW) were used for analysis of the data which was not normally distributed. The rates and proportions were analyzed by Chi-square test (χ^2). The Pearson Product Moment Correlation was used for running the correlations.

Results

Description of the study subjects

As shown in (Table 1), the total study subjects were 130 patients with ACS, of whom 81 were males and 49 females, aged between 32 and 82 years with a median age of 58.0 (50.0 - 65.0) years. As risk factors, the frequency of diseases associated ACS were as follows; hypertension (HTN) 49.2%, diabetes mellitus (DM) 43.8%, HTN/DM, 25.4% (33/130) and dyslipidemia 11.5%. While frequency of family history of ACS was 7.7% and of smoking was 24.6%. The average hematological indices for all subjects were; hemoglobin (Hb), 13.4 ± 1.5 g/dl, total white blood cells count (TWBC), 7.75, 6.4 - 10.0 x 10^9/L and platelets 282.2 ± 84.8 x 10^9/L. However, the female patients had significantly lower Hb (p<0.001) and platelet (PLT) count (p 0.037) compared to males, but had comparable TWBC (p 0.379), (Table 2).

Variables	UA	NSTEMI	STEMI	p (χ^2)	All ACS
Number	23 (17.7%)	49 (37.7%)	58 (44.6%)		130 (100%)
Sex (M:F)	43.5% (10/13)	59.2% (29/20)	72.4% (42/16)	0.045	81/49
Age Median (25-75%) Range Categories (i; ii; iii)	 57.0, 50.0-64.5 45 – 75 0; 15; 8	 60.0, 53.5-65.3 34 – 77 1; 26; 22	 57.0, 46.0-65.0 32 – 82 6; 29; 23	 0.388 ≠	 58.0, 50.0 - 65.0 32.0 - 82.0 7; 70; 53
HTN	56.5% (13/23)	57.1% (28/49)	39.7% (23/58)	0.146	49.2% (64/130)
DM	43.5% (10/23)	42.9% (21/49)	44.8% (26/58)	0.979	43.8% (57/130)
HTN/DM	7	12	14		
Dyslipidemia:	17.4% (4/23)	8.2% (4/49)	12.1% (7/58)	0.513	11.5% (15/130)
Family history	13.0% (3/23)	4.1% (2/49)	8.6% (5/58)	0.387	7.7% (10/130)
Smoking	4.3% (1/23)	24.5% (12/49)	32.8% (19/58)	0.028	24.6% (32/130)
Hb (g/dl)	12. 8 ± 1.8	13.4 ± 1.5	13.6 ± 1.5	0.089 ∗	13.4 ± 1.5
TWBC (x10^9/L)	6.0, 4.8-7.2	8.1, 6.3-10.3	8.7, 7.2-10.0	<0.001≠	7.75, 6.4 - 10.0
Platelets (x10^9/L)	275.0±106.2	298.0± 93.2	271.7±65.2	0.255∗	282.2 ± 84.8
Gensini score	10.0, 5.0-23.0	40.0, 15.8-60.5§	42.5,12.0-71.0§	0.002	33.5, 10.0-60.0
NLR	0.9, 0.8-1.1	2.9, 1.5- 3.8ø	3.5, 1.6-4.6ø	<0.001	2.55,1.2-3.9

Acute coronary syndrome pattern:

The frequencies of the three clinical types of ACS, the unstable angina (UA), non-ST-segment elevation myocardial infarction (NSTEMI), and STEMI, were 17.7%, 37.7%, and 44.6%, respectively (Table 1). While the vast majority of the STEMI were males (72.4%), majority of the UA were females 56.5% and of the NSTEMI were males (59.2%). Although the NSTEMI patients were slightly older, the 3 groups of patients were comparable in age, p 0.388, KW. Notably, all the UA patients were ≥ 45 yrs. Furthermore the Hb and platelet count were comparable between the three groups with slightly lower Hb in UA and platelet in STEMI, p 0.089 and p 0.255, respectively, however, the TWBC was significantly higher in STEMI, followed NSTEMI compared to UA, p <0.001.

Acute coronary syndrome risk factors and sex:

The potential risk factors, HTN, DM, combined HTN/DM, dyslipidemia and family history of ACS were comparable between the 3 clinical groups, UA, NSTEMI and STEMI except for cigarette smoking which was significantly higher in STEMI, followed by NSTEMI compared to UA, p 0.028, as shown in (Table 1). However, most of the risk factors were significantly different between the male and females patients. Females compared to males had significantly more frequent HTN (p 0.021), DM (p 0.011), HTN/DM (p 0.035) and dyslipidemia (p 0.006), on the contrary males were significantly more frequent smokers (p<0.001), while the family history IHD was comparable between the two sexes (Table 2).

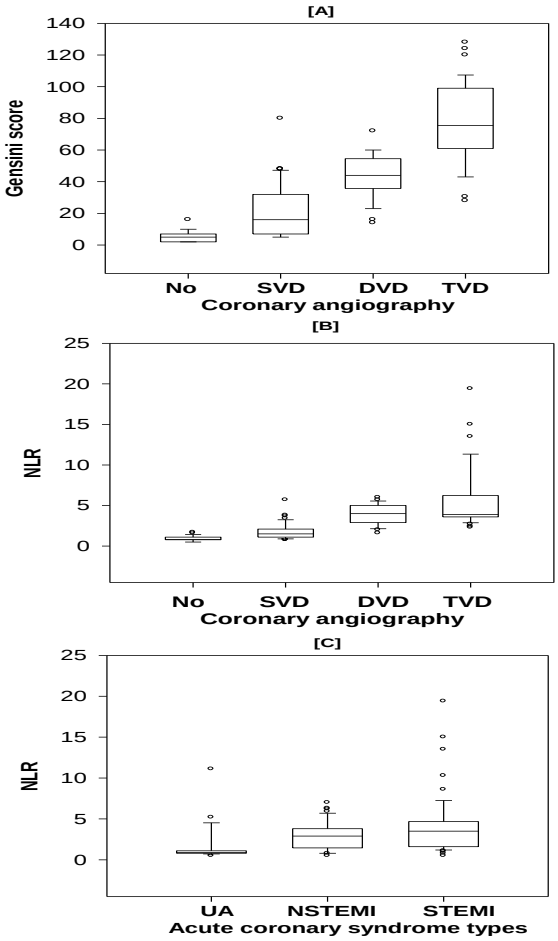
Variables	Males	Females	p (χ^2)

Number	81 (62.3%)	49 (37.7%)	<0.001
Age			
Median (25-75%)	60.0, 50.8 - 70.0	56.0, 50.0 - 65.0	0.083≠
Range	32 - 82	32 - 80	
Categories (i; ii; iii)	6:36:39	1:34:14	
HTN	40.7% (33/81)	63.3% (31/49)	0.021
DM	34.6% (28/81)	59.2% (29/49)	0.011
HTN/DM	18.5% (15/81)	36.7% (18/49)	0.035
Smoking	38.3% ((31/81)	2.0% (1/49)	<0.001
Dyslipidemia:	4.9% (4/81)	22.4% (11/49)	0.006
Family history	9.9% (8/81)	4.1% (2/49)	0.389
Hb (g/dl)	13.7, 12.6 - 14.9	13.0, 12.3 - 13.5	<0.001≠
TWBC ($x10^9$/L)	7.9, 6.6 - 10.0	7.5, 6.0 - 9.55	0.379≠
Platelets ($x10^9$/L)	270.1 ± 74.3	302.1 ± 97.2	0.037*
NLR	2.6, 1.38 - 3.9	2.3, 0.98 - 4.13	0.293≠
Gensini score	40.0, 13.5 - 60.0	28.0, 6.75 - 53.75	0.304≠
ACS type			
Unstable angina	12.3% (10)	26.5% (13)	
NSTEMI	35.8% (29)	40.8% (20)	0.045
STEMI	51.9% (42)	32.7% (16)	

Concordance of the coronary angiography (CAG) findings, Gensini score and the neutrophils/ lymphocytes ratio (NLR)

The Gensini score is a numerical estimation of the overall degree of ischemia and thus ACS severity, which was worked out from the visible angiographic findings, it was calculated based on the numbers and locations of stenosis in coronary arteries. The CAG showed, single vessel disease in 43 (33.1%) patients, three vessels disease in 38 (29.2%) patients, two vessels disease in 26 (20%) patients and non-significant CHD in 23 (17.7%) patients (data not shown).

As shown in (Fig. 1A), the Gensini score was markedly significantly different between patients with no (5.0, 2.25-6.75) or with single, (16.0, 7.25-30.0) double (44.0, 36.0-54.0) or triple (75.5, 62.0-99.0) coronary artery lesion regardless of the degree or location of stenosis, or the affected artery, $p<0.001$, KW.



Figures legends:

Figure 1. Grouping of patients with acute coronary syndrome (ACS), based on cardiac angiography (CAG), into patients with; no significant stenosis (No), single vessel disease (SVD), double vessel disease (DVD) and three vessel disease (TVD). A. Comparison of the median Gensini score showed marked difference between the four CAG groups, $p<0.001$, KW. B. Comparison of the median NLR (neutrophils/lymphocytes ratio), similarly showed marked difference between the four CAG groups, $p<0.001$, KW. C. Comparison of the median NLR between the ECG-based clinical groups of ACS, UA (unstable angina), NSTEMI (non-ST-segment elevation myocardial infarction) and STEMI, equally showing marked significant differences, $p<0.001$. In all figures the horizontal line within the box is the median while the bottom and top lines are the 25% - 75% percentiles, the lower and upper caps of the vertical lines are the 5% and 95% percentiles, while the open circles are outliers.

Interestingly, the NLR was similarly markedly significantly different between the patients in the same above 4 angiographic groups, patients with no stenosis (0.8, 0.78-1.08), single (1.5, 1.13-2.05), double (4.0, 2.9-4.9) or triple (3.9, 3.6-6.2) coronary artery lesion, $p<0.001$, KW (Fig. 1B).

Finally, the ROC curve defined NLR cut-off value of atherosclerosis to be 2.2, with 88.89% sensitivity, and 91.38% specificity (data not shown).

The association of the NLR with the acute coronary syndrome types

The median NLR values were significantly different between the ACS clinical types, it was highest in STEMI (3.5, 1.6-4.6), followed by NSTEMI (2.9, 1.48-3.8) and lowest in UA (0.9, 0.8-1.1), $p<0.001$, KW, (Fig 1C). Further, the TWBC was similarly differed between the type of the ACS with the highest count in STEMI (8.7, 7.2-10.0), followed by NSTEMI (8.1, 6.3-10.3) and lowest in UA (6.0, 4.8-7.2), $p<0.001$, KW, unlike the PLT count which was comparable between the 3 clinical groups, p 0.255 (Table 1).

The correlations of Gensini score with NLR and individual hematological parameters

As shown in (Fig. 2) there was statistically significant positive correlation between the NLR and Gensini score, i.e., as the Gensini score increased the NLR was equivalently increased, CC 0.671, $p<0.001$, Pearson Product Moment Correlation. Similarly, the neutrophils (CC 0.622, $p<0.001$), and TWBC (CC 0.366, $p<0.001$) were significantly positively correlated with Gensini score, while the lymphocytes counts were significantly negatively correlated with the Gensini score (CC-0.509, $p<0.001$), however, the PLT counts were not correlated with Gensini score (CC. -0.0796, p 0.368 - data not shown).

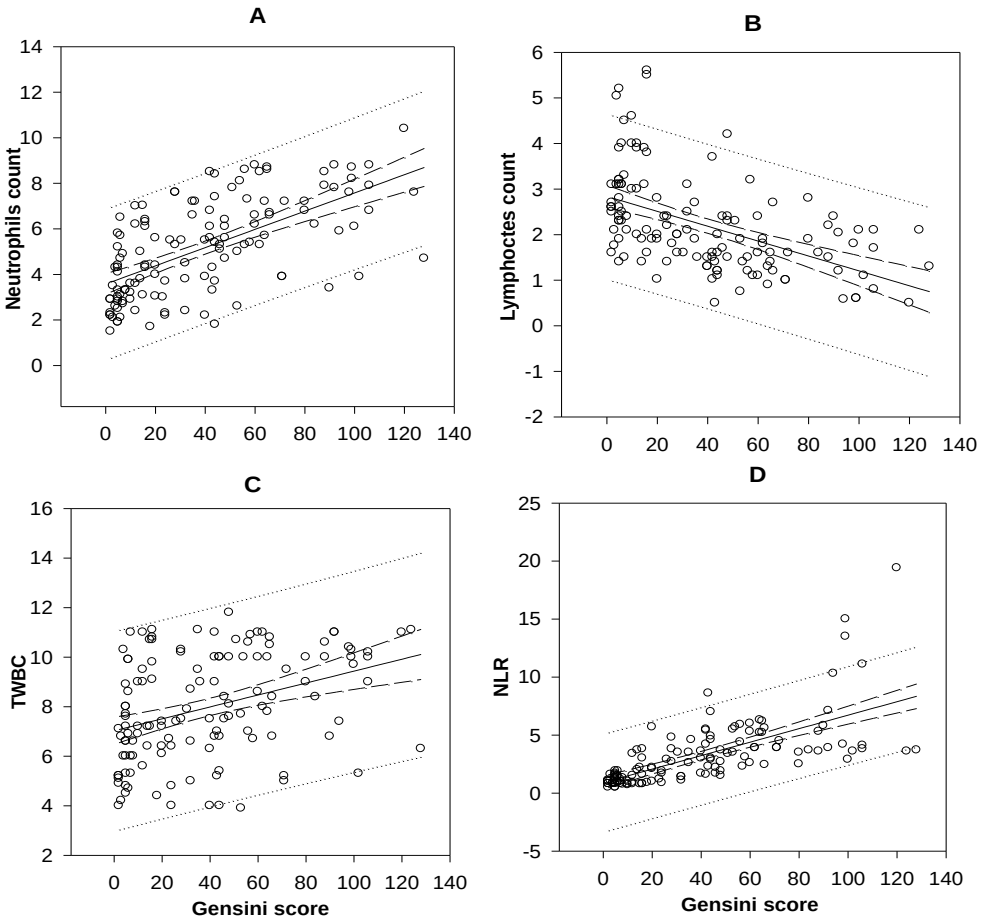


Figure 2. *Correlation of the Gensini score with hematological parameters, A. neutrophils (CC 0.622, p <0.001) B. lymphocytes (CC -0.509, p <0.001), C. total white blood cells – TWBC (CC 0.366, p <0.001) and neutrophils/lymphocytes ratio –NLR (CC 0.671, p <0.001), Pearson Product Moment Correlation. Note figure is present as regression analysis, to show, median, 25-75 percentiles and 5 – 95 percentiles, represented by the central line, surrounding upper and lower lines and outermost upper and lower lines, respectively, in addition to the individuals' data points represented by the open circles. The platelet data not shown in the graph, (CC -0.0796. p 0.368).*

Discussion

This study aimed to describe the clinical pattern and risk factors of ACS in the main cardiac center in Sudan, and furthermore to evaluate the NLR as simple affordable non-invasive indicator for disease severity as compared to Gensini score.

Age and sex are two important variables in ACS, in this study most of the patients (62.3%) were males, with an overall average age of presentation of 58 years, nevertheless, 53.8% of the patients were aged between 40-60 years, an age related to structural changes in arteries [19]. As expected, women present earlier (median age of 56 yrs.), compared to men (60 yrs.), and as small as 32 yrs. old patients were seen among both men and women (Table 2), as noticed somewhere else [20]. Unexpectedly, while the median age for NSTEMI was 60 yrs., the median age in both STEMI and UA was 57 yrs., but a large sample study was previously declared that older people are more likely to develop NSTEMI than STEMI [21].

This study disclosed the fact that the vast majority (82.3%) of patients diagnosed with ACS were had myocardial infarction (USTEMI and STEMI) i.e., cardiac necrosis, while the remainders had myocardial ischemia due to UA. Additionally, the more sever MI, the STEMI, was the more frequent (45%), which was consistent with what was reported before [22]. Furthermore, all patient were underwent cardiac angiography (CAG), almost half of the patients had 2 or more coronary arteries with significant stenosis. As seen in (Fig. 1A), the Gensini score of 5.0, 16.0, 44.0 and 75.5, was reflecting angiographic classification; no significant stenosis, single (SVD), double (DVD) and three (TVD) vessel diseases, respectively, p<0.001. This marked differences of the Gensini score showed strong concordance with CAG findings, but there was no wonder since the former is built on the latter findings [18]. Although the CAG-dependent Gensini scoring was generally consistent with the ECG-based clinical classification of ACS (UA, NSTEMI and STEMI), with increasing score of the former coincided with increasing severity in the latter, *p* 0.002, the Gensini score failed to distinguish between NSTEMI and STEMI, *p* 0.639, (Table 1).

The role of inflammation in atherosclerosis pathology and CVDs, and characterization of the latter as a chronic low-grade inflammatory conditions are now largely accepted [23, 24]. Of the markers of inflammation, the leukocytes (WBCs), namely neutrophils and lymphocytes [14]. In this study we noticed increased numbers of circulating TWBC and neutrophils on the contrary decreased lymphocytes, in patients with severe ACS (Table 1), as well as there were positive correlations of the TWBC and neutrophils and negative correlation of the lymphocytes with Gensini score, the ACS severity marker (Fig. 2). The NLR, which integrates the neutrophils and lymphocytes into a single biomarker, was found to be strong predictor for the ECG-dependent ACS clinical severity, in the present study. The NLR

increment was more pronounced in the STEMI followed by NSTEMI compared to UA, in line with previous studies [13, 14). The NLR like the Gensini score, was also failed to distinguish between the NSTEMI and STEMI, *p* 0.154, (Table 1). However, the NLR was markedly positively correlated with the Gensini score (Fig. 2D), as reported before [11, 25]. The parallel increase of both markers as indicators for increased ACS severity was recognized in different sites [26, 27]. Although healthy control subject were not included in the present study, a previous study showed that, NLR was significantly higher in CVD patients than in normal subjects, as well as it varied according to ethnicity [28].

Despite the well established relationship between NLR and atherosclerosis, the association between NLR and complexity of the coronary arteries stenosis is rarely investigated [29]. In this study, the NLR was also varied significantly with the CAG findings, as the NLR was almost 4 times higher in patients with double (DVD) or three (TVD) coronary arteries stenosis/disease as compared to patients with non-significant arterial stenosis, and around three times higher compared to patients with single artery stenosis (SVD), Fig. (1B). Similar results were reported before [29, 30], although another study, debated this relationship [31].

However, of the limitations of the NLR use as a biomarker for ACS is the versatile non-specific nature of the inflammatory markers in general. A systematic review and meta-analysis showed that high NLR was significantly associated with all CVD outcomes including CAD, ACS, stroke, and composite CVEs [32]. Thus, for use in ACS the NLR need to be coupled with other investigations and suggestive clinical evidences.

In the present study seven risk factors for IHD, including sex were tested. The higher incidence of ACS in men compared with women over the study period was evident (Table 2), which is a well-known testimonial [33]. In this study, HTH was found to be the most common risk factor (49.2%) followed by DM (43.8%), smoking (24.6%), then dyslipidemia (11.5%) and finally family history of IHD (7.7%). However, in a large European study dyslipidemia was found to be the highest risk factor followed by HTN [22], however, in another study, smoking was found to be the commonest risk factor [33]. Chronically, HTN is implicated in atherosclerosis by damaging the blood vessel walls and possibility of plaque deposition. Alternatively, the high prevalence of HTN in general population in different regions including Sudan [34, 35], which is by far overweighing the ACS prevalence, gives false impression that HTN is the predominant IDH risk factor. Although, the above variables are well established risk factors for ACS [36], in the present study the frequency of these factors, except smoking, were not significantly different between the clinical types of ACS, the UA, NSTEMI and STEMI (Table 1). Interestingly, when splitting the patient into males and females, the above factors, except the family history, were found to show differential frequencies between men and women and probably being stronger risk factors for ACS in one sex more than the other (Table 2). Thus, HTN, DM, HTN/DM and dyslipidemia were likely to derive towards ACS in women more than in men, while smoking derive oppositely. As it stand, men probably bears an unidentified stronger risk factor/s than the mentioned ones since the prevalence of the IHD is significantly higher in men.

Finally, in the present study, the calculated NLR cut-off point for atherosclerosis was found to be >2.2. However there are several different approaches e.g. Interactive Dot Plot, were used to define the cu-off points for different goals with different values [11, 37]. In this setting, the NLR cut-off value of 2.2 was set to be used as a predictor of severity of atherosclerosis. Of the limitations of this study, the relatively small sample size and lack of healthy controls, as well as, other acute inflammation markers such as CRP, hs-CT, serum amyloid A, were not tested.

In conclusion, this study described the clinical pattern of ACS and highlighted the differences of the order of the traditional risk factors of IHD between the local and global orders and between sexes. The vast majority of patients had STEMI and NSTEMI, most of them were males with a median age for ACS of 58 years. HTN, DM and dyslipidemia, in this order, were more strongly associated with ACS in women while smoking was the main risk factor in men. The NLR was in strong concordance with the ECG-dependent clinical diagnosis, CAG findings and Gensini score, and proved to be a reliable indicator for ACS severity. The NLR cutoff value for ACS severity was found to be 2.2.

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Declarations

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Conflicts of interest/Competing interests: No conflict of interest for all authors to declare

Availability of data and material: The data is available upon genuine request

Code availability: 'Not applicable'

Authors' contributions (optional): 'Not applicable'

Ethics approval: The studies were ethically approved by the ethical committee of Sudanese medical speciation board (no reference number).

Consent to participate: An informed consent was obtained from each patient before inclusion in the study. The data was confidentially maintained

Consent for publication: Consent for publication was obtained.

References

1. WHO. Cardiovascular Diseases, 2021.
2. Smith JN, Negrelli JM, Manek MB, Hawes EM, Viera AJ (2015). Diagnosis and management of acute coronary syndrome: an evidence-based update. *J Am Board Fam Med*.;28(2):283-93. doi: 10.3122/jabfm.2015.02.140189. PMID: 25748771.
3. Maas AH, Appelman YE (2010). Gender differences in coronary heart disease. *Neth Heart J*. ;18(12):598-602. doi: 10.1007/s12471-010-0841-y. PMID: 21301622.
4. Kumar A, Cannon CP (2009). Acute coronary syndromes: diagnosis and management, part I. Mayo *Clin Proc*.;84(10):917-38.
5. Barstow C, Rice M, McDivitt JD. Acute Coronary Syndrome: Diagnostic Evaluation. Am Fam Physician,1;95(3):170-177. PMID: 28145667.
6. Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T, Sibbing D (2020). Siontis GCM; ESC Scientific Document Group. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. *Eur Heart J*. 2021
7. Sato A(2014). Coronary plaque imaging by coronary computed tomography angiography. *World J Radiol*.,28;6(5):148-59. doi: 10.4329/wjr.v6.i5.148. PMID: 24876919.
8. van der Wal AC, Becker AE (1999). Atherosclerotic plaque rupture--pathologic basis of plaque stability and instability. *Cardiovasc Res*.41(2):334-44. doi: 10.1016/s0008-

6363(98)00276-4. PMID: 10341833.
9. Badimon L, Padró T, Vilahur G (2012). Atherosclerosis, platelets and thrombosis in acute ischaemic heart disease. *Eur Heart J Acute Cardiovasc Care*.;1(1):60-74. doi: 10.1177/2048872612441582. PMID: 24062891.
10. Wolf D, Ley K (2019). Immunität und Entzündung bei Arteriosklerose [Immunity and inflammation in atherosclerosis]. Herz.;44(2):107-120. doi: 10.1007/s00059-019-4790-y. PMID: 30859253.
11. Li X, Ji Y, Kang J, Fang N (2018). Association between blood neutrophil-to-lymphocyte ratio and severity of coronary artery disease: Evidence from 17 observational studies involving 7017 cases. Medicine (Baltimore).;97(39):e12432. doi: 10.1097/MD.0000000000012432. PMID: 30278521.
12. Gurm HS, Bhatt DL, Lincoff AM, Tcheng JE, Kereiakes DJ, Kleiman NS, Jia G, Topol EJ (2003). Impact of preprocedural white blood cell count on long term mortality after percutaneous coronary intervention: insights from the EPIC, EPILOG, and EPISTENT trials. Heart.; 89(10):1200-4. doi: 10.1136/heart.89.10.1200. PMID: 12975419.
13. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS (2008). Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol.;102(6):653-7. doi: 10.1016/j.amjcard.2008.05.006. PMID: 18773982.
14. Ateş AH, Aytemir K, Koçyiğit D, Yalcin MU, Gürses KM, Yorgun H, Canpolat U, Hazırolan T, Özer N (2016). Association of Neutrophil-to-Lymphocyte Ratio with the Severity and Morphology of Coronary Atherosclerotic Plaques Detected by Multidetector Computerized Tomography. Acta Cardiol Sin.;32(6):676-683. doi: 10.6515/acs20160225a. PMID: 27899854.
15. Wang Z, Wang J, Cao D, Han L (2020). Correlation of neutrophil-to-lymphocyte ratio with the prognosis of non-ST-segment elevation in patients with acute coronary syndrome undergoing selective percutaneous coronary intervention. *J Int Med Res*.;48(10):300060520959510. doi: 10.1177/0300060520959510. PMID: 33050747.
16. Balta S, Celik T, Mikhailidis DP, Ozturk C, Demirkol S, Aparci M, Iyisoy A (2016). The Relation Between Atherosclerosis and the Neutrophil-Lymphocyte Ratio. Clin Appl Thromb Hemost.;22(5):405-11. doi: 10.1177/1076029615569568. PMID: 25667237.
17. Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M (2017). What is the normal value of the neutrophil-to-lymphocyte ratio? BMC Res Notes.;10(1):12. doi: 10.1186/s13104-016-2335-5. PMID: 28057051.
18. Avci A, Fidan S, Tabakçı MM, Toprak C, Alizade E, Acar E, Bayam E, Tellice M, Naser A, Kargın R (2016). Association between the Gensini Score and Carotid Artery Stenosis. *Korean Circ J*.46(5):639-645. doi: 10.4070/kcj.2016.46.5.639. PMID: 27721854.
19. Fleg JL, Strait J (2012). Age-associated changes in cardiovascular structure and function: a fertile milieu for future disease. Heart Fail Rev.;17(4-5):545-54. doi: 10.1007/s10741-011-9270-2. PMID: 21809160.
20. Ricci B, Cenko E, Vasiljevic Z, Stankovic G, Kedev S, Kalpak O, Vavlukis M, Zdravkovic M, Hinic S, Milicic D(2017). Acute Coronary Syndrome: The Risk to Young Women. *J Am Heart Assoc*.;6(12):e007519. doi: 10.1161/JAHA.117 .007519. PMID: 29273636.
21. Rosengren A, Wallentin L, Simoons M, Gitt AK, Behar S, Battler A, Hasdai D (2006). Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. *Eur Heart J*.;27(7):789-95. doi: 10.1093/eurheartj/ehi774. PMID: 16464911.
22. Montalescot G, Dallongeville J, Van Belle E, Rouanet S, Baulac C, Degrandsart A (2007), Vicaut E; OPERA Investigators. STEMI and NSTEMI: are they so different? 1 year outcomes in acute myocardial infarction as defined by the ESC/ACC definition (the OPERA registry). *Eur Heart J*.28(12):1409-17. doi: 10.1093/eurheartj/ehm031. PMID: 17412730.
23. Pai JK, Pischon T, Ma J, Manson JE, Hankinson SE, Joshipura K, Curhan GC, Rifai N(2004). Inflammatory markers and the risk of coronary heart disease in men and women. N Engl J Med.;351(25):2599-610. doi: 10.1056/NEJMoa040967. PMID: 15602020.
24. Golia E, Limongelli G, Natale F, Fimiani F, Maddaloni V, Pariggiano I, Bianchi R, Crisci M, D'Acierno L(2014). Inflammation and cardiovascular disease: from pathogenesis to therapeutic target. Curr Atheroscler Rep.16(9):435. doi: 10.1007/s11883-014-0435-z. PMID: 25037581.
25. Yang Y, Xu Y, Wang J, Zhai X, Jiang H (2020). Predictive efficacy of neutrophil ‐ to ‐ lymphocyte ratio for long ‐ term prognosis in new onset acute coronary syndrome : a retrospective cohort study. BMC Cardiovasc Disord [Internet].;1–11.
26. Neeland IJ, Patel RS, Eshtehardi P, Dhawan S. Interventional Cardiology Coronary angiographic scoring systems : An evaluation of their equivalence and validity. *Am Heart J*
27. Chen J, Chen MH, Li S, Guo YL, Zhu CG, Xu RX (2014). Usefulness of the neutrophil-to-lymphocyte ratio in predicting the severity of coronary artery disease: a Gensini score assessment. *J Atheroscler Thromb*.21(12):1271-82.
28. Azab B, Camacho-Rivera M, Taioli E (2014). Average values and racial differences of neutrophil lymphocyte ratio among a nationally representative sample of United States subjects. PLoS One. Nov 6;9(11):e112361.
29. Sharma K, Patel AK, Shah KH, Konat A (2017). Is Neutrophil-to-Lymphocyte Ratio a Predictor of Coronary Artery Disease in Western Indians? *Int J Inflam*.2017:4136126. doi: 10.1155/2017/4136126. PMID: 28811954.
30. Zhou D, Wan Z, Fan Y, Zhou J, Yuan Z (2015). A combination of the neutrophil-to-lymphocyte ratio and the GRACE risk score better predicts PCI outcomes in Chinese Han patients with acute coronary syndrome. *Anatol J Cardiol*.;15(12):995-1001. doi: 10.5152/AnatolJCardiol.2015.6174. PMID: 26663224.
31. Diniz LR, de Lima SG, de Amorim Garcia JM, de Oliveira Diniz KL (2019). Neutrophil to Lymphocyte Ratio as a Prognostic Predictor in Older People with Acute Coronary Syndrome. Angiology.70(3):264-271. doi: 10.1177/0003319718796565. PMID: 30153747.
32. Angkananard T, Anothaisintawee T, McEvoy M, Attia J, Thakkinstian A (2018). Neutrophil Lymphocyte Ratio and Cardiovascular Disease Risk: A Systematic Review and Meta-Analysis. *Biomed Res Int*.;2018:2703518. doi: 10.1155/2018/2703518. PMID: 30534554.
33. Hubacek JA, Stanek V, Gebauerova M, Adamkova V, Lesauskaite V, Zaliaduonyte-Peksiene D, (2017). Traditional risk factors of acute coronary syndrome in four different male populations - total cholesterol value does not seem to be relevant risk factor. Physiol Res.;66(Suppl 1):S121-S128. doi: 10.33549/physiolres.933597. PMID: 28379037.
34. Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM (2016). Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. Circulation.;134(6):441-50. doi: 10.1161/CIRCULATIONAHA.115.018912. PMID: 27502908.
35. Beheiry HM, Abdalla AA, Fahal NA, Mohamed MI, Ibrahim DA,

Medani SA, Khalfa HA, Poulter NR (2020). May Measurement Month 2018: an analysis of blood pressure screening results from Sudan. *Eur Heart J Suppl*.22(Suppl H):H122-H124. doi: 10.1093/eurheartj/ suaa045. PMID: 32884490.

36. James, S., Pedersen, L, & Prescott, E (2021). (2018-12). General risk factors of acute coronary syndromes. In ESC CardioMed. Oxford, UK: Oxford University Press. Retrieved 12 Apr.
37. Dong CH, Wang ZM, Chen SY (2018). Neutrophil to lymphocyte ratio predict mortality and major adverse cardiac events in acute coronary syndrome: A systematic review and meta-analysis. Clin Biochem.;52:131-136. doi: 10.1016/j.clinbiochem.2017.11.008. PMID: 29132766.

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