ORIGINAL RESEARCH ARTICLE

Evaluation of Neutrophil Lymphocyte Ratio and Platelet to Lymphocyte Ratio in Patients with Peripheral Vascular Disease Undergoing Endovascular Management

Abhinav Amarnath Mohan[1], Pankaj Jawahar Banode[2]

[1]Assistant Professor, [2]Professor, Department of Radiology, TIFAC-CORE Interventional Radiology (A.V.B.R.H.) D.M.I.M.S. Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, India

Corresponding author: Dr Abhinav Amarnath Mohan, Assistant Professor, Department of Radiology, TIFAC-CORE Interventional Radiology (A.V.B.R.H.) D.M.I.M.S., Jawaharlal Nehru Medical College, Sawangi (Meghe), Wardha, India

How to cite this article: Abhinav Amarnath Mohan, Pankaj Jawahar Banode. Evaluation of neutrophil lymphocyte ratio and platelet to lymphocyte ratio in patients with peripheral vascular disease undergoing endovascular management. International Journal of Contemporary Medicine Surgery and Radiology. 2017;2(4):117-123.

ABSTRACT

Introduction: With improvement in quality of life and per capita income in developing countries there has been a gradual shift and rising trend of non-communicable diseases including coronary artery diseases and peripheral vascular diseases. Study aimed **t**o calculate and evaluate from Complete Blood Count (CBC), the Neutrophil Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) in patients presenting with PVD undergoing endovascular management in department of Interventional Radiology (I.R.), to study Association of N.L.R (3.95) and P.L.R (< 150 and >150) with Rutherford's clinical presentation criteria and to study Association of N.L.R (3.95) and P.L.R (< 150 and >150) with post I.R endovascular management and prognostic outcomes in terms of Amputation and amputation free survival.

Material and Methods: This study was a prospective observational study comprising of 44 patients who were referred to interventional radiology department over a period of 8 months. A detailed history was taken in all patients followed by thorough clinical examination. Complete and differential blood count was done and PLR and NLR were determined in all patients. The association of PLR and NLR with amputation free survival, necessity for major amputation and Rutherford clinical classification was studied.

Results: Our study comprised of 44 patients out of which 37 were males 7 were females with a M:F ratio being 1:0.18. The mean age of patients in our study was 55.04 +/- 14.12 with distribution between 23 to 84 years. Statistically significant correlation was found between NLR and PLR with major amputation, amputation free survival and Rutherford clinical classification. In this study NLR and Rutherford's clinical classification were most significant parameters with respect to peripheral vascular disease and critical limb ischemia in terms of clinical staging, prognostication and outcome prediction.

Conclusion: Our study had significant multidimensional outcomes in terms of clinical as well as short and long term implications in management of PVD and endovascular interventions utilizing N.L.R and P.L.R.

Key words: Complete Blood Count (CBC), Neutrophil Lymphocyte Ratio (NLR), Platelet to Lymphocyte Ratio (PLR), Peripheral Vascular Disease (PVD), Critical Limb Ischemia (CLI), endovascular management.

INTRODUCTION

Similar to developed countries in India there is a shift and rising trends of non-communicable diseases over the previously prevalent communicable diseases in community.[1] The majority of non-communicable diseases showing upward trends in India are neoplastic, cardiovascular, autoimmune and peripheral vascular diseases.[2] Unfortunately many of these non-communicable diseases particularly peripheral vascular diseases show ice berg phenomenon i.e. only a small portion of affected will actually seek proper medical attention and large asymptomatic population in the community remains undetected. The large undetected burden of the disease usually belongs to rural population with lack of access to medical facilities. This population has to suffer from the burden of increased morbidity and mortality.[3]

The morbidity and mortality due to peripheral vascular disease has significant implications not only for the individual himself but also for the family and society as a whole especially in regards to economic, psycho-social and to nation in form of disability adjusted life years (DALYs) and lost man-hours to productive work thus causing significant effect on growth as well as excess burden on economy.[4] One of the complications of peripheral vascular

disease includes critical limb ischemia which is usually due to compromised blood supply to limb secondary to arteriosclerotic plaque and thrombus.[5] This critical limb schema may produce symptoms like intermittent claudication, numbness and eventually rest pain. Severe Ischemia may present as non-healing ulcers and gangrene resulting into need for amputation.[6] Various imaging techniques like peripheral doppler and CT angiography may aid in the diagnosis. Once the diagnosis is established the treatment modality may include by-pass surgeries or endovascular treatment.[7] Endovascular treatment though highly effective may not be available for a vast majority of population in developing countries due to various reasons.[8] The rural population has to bear heavy toll due to non- availability of advanced medical treatments like interventional radiology that can be helpful in prevention of amputation or aid in downgrading the level of high amputation or major amputation by timely endovascular interventions to a significant extent. The Neutrophil Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) have been easily derived from basic laboratory investigation i.e. CBC (Complete Blood Count). Role of Neutrophil as marker of Acute inflammation as well as associated with atherosclerotic lesion and Platelets playing key role in atherosclerosis and atherothrombosis have been already outlined. The elevated NLR and PLR have been found significant associations with oncologic and cardio-vascular disorders in many research articles. The association of NLR and PLR with Critical limb ischemia in peripheral vascular diseases have been published by many randomized controlled trials.[9,10]

Our prospective study undertaken in rural hospital especially serving rural population as pilot study had significant multidimensional outcomes in terms of clinical as well as both long term and short term implications in management of peripheral vascular disease and endovascular interventions that will be highlighted in details subsequently. We undertook this project because of significance of importance proven by published studies of this readily available, inexpensive basic laboratory investigation of Complete Blood Counts. Our emphasis was to establish the role of NLR and PLR as outlined in our objectives in Indian scenario in rural hospital interventional radiology department of our esteemed institute as pilot study in rural hospital.

MATERIAL AND METHODS

This was a Prospective observational study. Diagnosed patients of Peripheral vascular disease or critical limb ischemia who presented to Interventional radiology department of our institution over a period of 1 year were included in this study. The study was part of a project for fellowship in Interventional radiology curriculum.

All the patients were evaluated for Complete Blood Count (C.B.C.) with Differential Count, clinical signs/symptoms and classification scores like Rutherford classification for PVD/CLI, prior to endovascular treatment and after the procedure (at the time of discharge). All the included Cases underwent Conventional Angiogram – Arteriogram and Interventional Endovascular procedure; which was performed with Digital Subtraction Angiography (D.S.A.) Machine by Philips Model :Allura FD20 advanced Cath Lab System. Appropriate investigations and consultations (physician's opinion, anesthetic fitness, surgery opinion if required etc) were done before endovascular intervention. DSA Technique In Diagnostic Angiography (cardiac and vascular mode acquisitions.) were undertaken. Endovascular Management Approach and Techniques consisted of different procedures depending upon the case and included Angioplasty (POBA), Angioplasty with Stenting, Intra-Arterial Thrombolysis (IAT), Directional atherectomy and Percutaneous Catheter Techniques (Penumbra Device /Aspiration, Mechanical Thrombolytic, or Thrombolytic Therapy). In all patients the outcome at discharge and follow and prognosis up was studied. The study was approved by institutional ethical committee. Informed consent taken from all the patients.

Inclusión Criteria

1) Patient who have been clinically diagnosed /screened /diagnosed on colour Doppler/Contrast CT/ MRI (reports from outside/from us) with Peripheral Vascular Disease / Critical Limb (CLI).
2) Those undergone Digital subtraction Angiography (D.S.A) and endovascular treatment in our interventional radiology department.

Exclusion Criteria

1) Symptomatic cases due to Trauma (Road Traffic Accident) those patients not undergoing endovascular management.
2) Patients having allergy to contrast.
3) Patients not giving informed consent.

STATISTICAL ANALYSIS

Statistical analysis was done by using descriptive and inferential statistics using Pearson's Correlation coefficient, Chi-square Test, Odd's Ratio and Multivariate Regression Analysis and software used in the analysis were SPSS 17.0 version, Graph Pad Prism 6.0 version and EPI-INFO 6.0 version and $p < 0.05$ is considered as level of significance(). The estimated required sample size by appropriate statistical method was 43 cases and our study comprised of 44 cases hence our sample size was found to be adequate.

RESULTS

The study population consisted of 44 patients who have been clinically or with the help of appropriate imaging technique were diagnosed to be having PVD, CLI and were referred to our institute for endovascular treatment.

Out of the 44 studied cases 37 were males and 7 were females with an M: F ratio being 1:0.18 (figure-1).

Mean age of patients in our case study was 55.04 +/- 14.12 with distribution between 23 to 84 years; with 25% each in age range of 51 to 60 years and 61to 70 years with another 11% in 71-80 years age group thus staggering to over 60% cases. In this study there was a significant correlation between NLR and PLR with Pearson's correlation coefficient value 'r' of 0.743 with p- value of 0.0001 which was found to be statistically significant (table-1).

The study population was categorized according to the NLR into 2 tertiles first tertile (NLR </= 3.95) and second tertile (median NLR > 3.95) patients were studied for various factors like need for amputation, amputation free survival, major or minor amputation and presence of major risk factors for development of PVD or CLI. Chi square test and P values were determined to find out presence of statistically significant difference on the basis of NLR. There was statistically significant association between NLR and amputation (P=0.0001), amputation free survival (P=0.0001), major amputation (P=0.0001) and Rutherford classification (P=0.0001) (table-2).

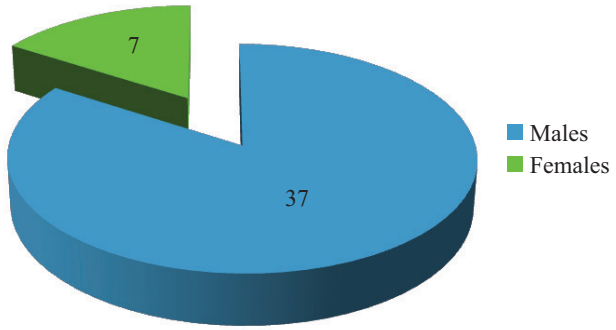

Figure-1: Gender Distribution of the studied cases.

Next the study population was categorized according to the PLR into 2 tertiles first tertile (PLR </= 150) and second tertile (median PLR> 150) patients were studied for various factors like need for amputation, amputation free survival, major or minor amputation and presence of major risk factors for development of PVD or CLI. Chi square test and P values were determined to find out presence of statistically significant difference on the basis of NLR. There was statically significant association between PLR and amputation (P=0.007), amputation free survival (P=0.004)(P=0.0001), and Rutherford classification (P=0.001) (table-3).

On univariate statistical analysis significant association was found between NLR and PLR as well as NLR and PLR with Rutherford's clinical classification and with cases having amputation and amputation free survival thus aiding in prediction of outcomes and prognosis as well as clinical staging (table-4). NLR (P=0.0001) was found to be more sensitive for major amputation than PLR (P=0.001) (figure-2).

In multiple logistic regressions for PVD and Rutherford's clinical classification category had significant association with p-Value of 0.042. Other factors like amputation, amputation free survival, debridement, major and minor amputations, Gender and cardiovascular risk factors were not found to be statistically significant (table-5).

Similarly multiple logistic regression for NLR and Rutherford's clinical classification category had significant association with p-Value of 0.040. Other factors like amputation, amputation free survival, debridement, major and minor amputations, Gender tobacco or smoking and

	Mean	Std. Deviation	N	Correlation 'r'	p-value
NLR	3.37	3.05	44	0.743	0.0001,S
PLR	135.22	96.87	44		

Table-1: Correlation between NLR and PLR

	NLR		⌘2-value	p-value
	NLR≤3.95	NLR>3.95		
Amputation	10(22.73%)	9(20.45%)	14.88	0.0001,S
Amputation Free Survival	26(59.09%)	0(0%)	16.34	0.0001,S
Debridement	12(27.27%)	1(2.27%)	1.84	0.17,NS
Major Amputation	5(11.36%)	8(18.18%)	19.14	0.0001,S
Minor Amputation	5(11.36%)	1(2.27%)	0.06	0.80,NS
Cardiovascular Risk Factors	20(45.45%)	6(13.64%)	0.26	0.60,NS
DM Type II	5(11.36%)	2(4.55%)	0.33	0.56,NS
Gender	29(65.91%)	8(18.18%)	0.19	0.65,NS
H/O Tobacco/ Smoking	27(61.36%)	5(11.36%)	1.68	0.19,NS
Rutherford Classification				
I	6(13.64%)	0(0%)	17.03	0.0001,S
IIa	23(52.27%)	1(2.27%)		
IIb	6(13.64%)	8(18.18%)		

Table-2: Clinical and hematological characteristics of population with NLR≤3.95and NLR > 3.95.

	PLR		⅄2-value	p-value
	PLR≤150	PLR>150		
Amputation	11(25%)	8(18.18%)	7.15	0.007,S
Amputation Free Survival	24(54.55%)	2(4.55%)	8.18	0.004,S
Debridement	11(25%)	2(4.55%)	0.56	0.45,NS
Major Amputation	8(18.18%)	5(11.36%)	2.60	0.10,NS
Minor Amputation	3(6.82%)	3(6.82%)	2.94	0.08,NS
Cardiovascular Risk Factors	18(40.91%)	8(18.18%)	2.34	0.12,NS
DM Type II	5(11.36%)	2(4.55%)	0.16	0.68,NS
Gender	29(65.91%)	8(18.18%)	0.16	0.68,NS
H/O Tobacco/ Smoking	27(61.36%)	5(11.36%)	1.05	0.30,NS
Rutherford Classification				
I	6(13.64%)	0(0%)	14.03	0.001,S
IIa	22(50%)	2(4.55%)		
IIb	6(13.64%)	8(18.18%)		

Table-3: Clinical and hematological characteristics of population with PLR≤150 and PLR>150.

	Rutherford Classification			Total	⅄2-value	p-value
	I	IIa	IIb			
NLR						
NLR≤3.95	6(13.64%)	23(52.27%)	6(13.64%)	35	17.03	0.0001,S
NLR>3.95	0(0%)	1(2.27%)	8(18.18%)	9		
Total	6(13.64%)	24(54.55%)	14(31.82%)	44		
PLR						
PLR≤150	6(13.64%)	22(50%)	6(13.64%)	34	14.03	0.001,S
PLR>150	0(0%)	2(4.55%)	8(18.18%)	10		
Total	6(13.64%)	24(54.55%)	14(31.82%)	44		

Table-4: Association of NLR and PLR with Rutherford Classification

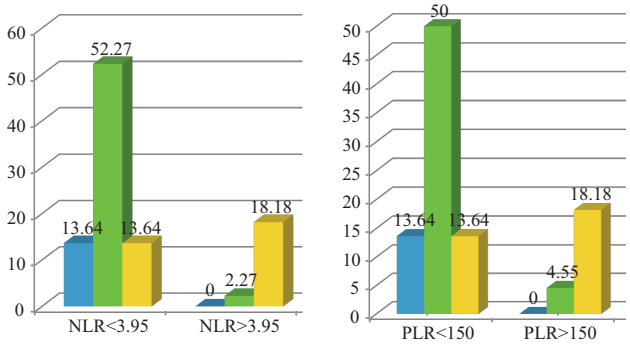

Figure-2: Association of NLR (Left) and PLR (Right) with Rutherford Classification

cardiovascular risk factors were not found to be statistically significant (table-6).

In multiple logistic regression for PLR and Rutherford's clinical classification category had not found to have significant association with p-Value of 0.109 (table-7).

DISCUSSION

Mean age of patients in our case study was 55.04 +/- 14.12 with distribution between 23 to 84 years; with 25% each in age range of 51 to 60 years and 61to 70 years with another 11% in 71-80 years age group thus staggering to over 60% cases. Similar findings were found in the studies done by Shammas NW et al (Mean Age 60 years), Aronow WS (Mean age 69 years) and Alzamora MT et al (61 years). Increase in age positively correlates with the incidence of peripheral arterial disease as seen in abovementioned studies.[11,12,13]

In our study 37 were males and 7 were females with a M:F ratio being 1:0.18. Similar findings were seen in studies conducted by Morris-Stiff G et al, Federman DG et al and Mark G. Davies et al. Initially the male predominance was attributed to increased incidence of smoking in males but increased incidence of peripheral arterial disease may also be related to factors like diabetes and insulin resistance, duration of diabetes, obesity and sedentary life style. It is generally accepted that incidence of peripheral vascular diseases increase as the duration of diabetes increases.[14,15,16]

The mean NLR value being 3.37 with standard deviation of 3.05 and that for PLR being 135.22 with std.deviation of 96.87. There was Statistically Significant Association Of NLR And PLR With Amputation With Odd's Ratio For NLR =46.14(95% CI=2.45-867.6) and PLR =8.36 (95% CI=1.51-46.17) With ⅄2-Value For NLR = 14.88 and PLR =7.15 While P-Value For NLR = 0.0001 and PLR = 0.007. There was Statistically Significant Association of NLR and PLR with Amputation free survival with ⅄2-Value for NLR = 16.34 and PLR =8.18 While P-Value for NLR = 0.0001 and PLR = 0.004. There was Statistically Significant Association of NLR and PLR with Rutherford clinical classification with ⅄2-Value for NLR = 17.03 and PLR =14.03 While P-Value for NLR =

	Unstandardized Coefficients		Odd's Ratio	t	p-value	95.0% Confidence Interval for B	
	B	Std. Error				Lower Bound	Upper Bound
PVD	-428.19	532.69		-	-	-1511.975	655.582
Amputation	68.66	90.71	0.355	0.757	0.455,NS	-115.907	253.232
Amputation free survival	100.15	148.65	0.514	0.674	0.505,NS	-202.295	402.596
Debridement	6.47	36.42	0.031	0.178	0.860,NS	-67.635	80.580
Major Amputation	-10.90	97.370	0.052	0.112	0.912,NS	-209.002	187.200
Minor Amputation	68.91	86.894	0.247	0.793	0.433,NS	-107.870	245.705
Cardiovascular Risk Factors	-45.77	33.03	0.235	1.386	0.175,NS	-112.984	21.438
DM Type II	56.19	38.38	0.215	1.464	0.153,NS	-21.903	134.285
Gender	-70.88	39.52	0.271	1.793	0.082,NS	-151.299	9.533
H/O Tobacco/ Smoking	64.79	37.91	0.301	1.709	0.097,NS	-12.354	141.934
Rutherford Classification	70.8	33.43	0.480	2.118	0.042,S	2.789	138.828

Table-5: Multiple logistic regression for PVD

	Unstandardized Coefficients		Odd's Ratio	t	p-value	95.0% Confidence Interval for B	
	B	Std. Error				Lower Bound	Upper Bound
NLR	0.717	1.956					
Amputation	0.052	0.333	0.064	0.156	0.877,NS	-0.626	0.730
Amputation free survival	0.070	0.546	0.085	0.128	0.899,NS	-1.041	1.180
Debridement	0.021	0.134	0.024	0.155	0.877,NS	-0.251	0.293
Major Amputation	-0.385	0.358	-0.435	1.077	0.289,NS	-1.112	0.342
Minor Amputation	0.080	0.319	0.068	0.252	0.803,NS	-0.569	0.729
Cardiovascular Risk Factors	-0.100	0.121	-0.122	0.826	0.415,NS	-0.347	0.147
DM Type II	0.181	0.141	0.164	1.285	0.208,NS	-0.106	0.468
Gender	-0.220	0.145	-0.200	1.518	0.138,NS	-0.516	0.075
H/O Tobacco/ Smoking	0.213	0.139	0.235	1.528	0.136,NS	-0.071	0.496
Rutherford Classification	0.262	0.123	0.422	2.133	0.040,S	0.012	0.512

Table-6: Multiple logistic regression for NLR

	Unstandardized Coefficients		Odd's Ratio	t	p-value	95.0% Confidence Interval for B	
	B	Std. Error				Lower Bound	Upper Bound
PLR	-1.654	2.525					
Amputation	0.134	0.430	0.158	0.311	0.758,NS	-0.741	1.009
Amputation free survival	0.620	0.705	0.728	0.881	0.385,NS	-0.813	2.054
Debridement	-0.067	0.173	-0.073	0.389	0.699,NS	-0.418	0.284
Major Amputation	0.370	0.462	0.403	0.802	0.428,NS	-0.569	1.309
Minor Amputation	0.183	0.412	0.150	0.444	0.660,NS	-0.655	1.021
Cardiovascular Risk Factors	-0.118	0.157	-0.139	0.756	0.455,NS	-0.437	0.200
DM Type II	0.170	0.182	0.149	0.935	0.356,NS	-0.200	0.540
Gender	-0.113	0.187	-0.099	0.602	0.551,NS	-0.494	0.268
H/O Tobacco/ Smoking	0.279	0.180	0.296	1.552	0.130,NS	-0.087	0.645
Rutherford Classification	0.261	0.158	0.404	1.646	0.109,NS	-0.062	0.583

Table-7: Multiple logistic regression for PLR

0.0001 and PLR = 0.001. There Is Statistically Significant Association of NLR With major amputation with ϰ2-Value for NLR = 19.04 with P-Value of 0.001. Similar conclusions were drawn in the studies conducted by Bhat TM et al, TM Bhat et al and Yang J et al.[17,18]

Thus on univariate statistical analysis there is found to be significant association between NLR and PLR as well as NLR and PLR with Rutherford's clinical classification and with cases having amputation and amputation free survival thus aiding in prediction of outcomes and prognosis as well as clinical staging; with NLR being more sensitive for major amputation. In multiple logistic regression for PVD; Rutherford's clinical classification category had significant association with p-Value of 0.042. Similarly multiple logistic regression for NLR; Rutherford's clinical classification category had significant association with p-Value of 0.040. Thus in our study NLR and Rutherford's clinical classification were most significant parameters in consideration with respect to PVD/CLI and in terms of clinical staging, prognostication and outcome prediction.

Similar findings were seen in studies conducted by Hardman RL and Swaminathan A.[19,20]

It is well established fact that Neutrophils have important role in formation of atherosclerotic plaques with lipid deposition and their progression. From CBC, the NLR is calculated using absolute neutrophils and lymphocyte counts. Amongst leucocytes: the neutrophils lead to inflammatory processes with release of arachidonic acid metabolites and platelet activating factors, while oxidative -stress cause relative lymphopenia through cortisol release. In one study Iso Y et al. investigated the impact of implanted bone marrow cell composition on limb salvage in patients with CLI. In this study lymphocytes were significantly elevated in the limb salvage group one possible explanation for this finding is the fact that lymphocytes might also be associated with the mediation of collateral growth via IL-16 secretion as was shown in a murine hindlimb ischemia model. Thus going through vast literature and published studies similar findings in our study are relevant, as patients with a high lymphocyte count, leading to a lower NLR might have more collateral growth leading to less ischemia and therefore less CLI leading to amputation free survival post endovascular procedure. Also during review of literature; another published paper revealed high CHA2DS2-VASc (congestive heart failure, hypertension, age75 years (doubled), type 2 diabetes, previous stroke, transient ischemic attack, or thromboembolism (doubled), vascular disease, age 65 to 75 years, and sex category) score was associated with a high risk for CLI in PVD patients; which are similar to our findings. Platelets further increase in response to ongoing inflammation; as could be found in patients with active atherosclerosis leading to a more aggressive course of their disease.[21, 22, 23, 24]

In our patients the median NLR and PLR was significantly associated and higher in patients with ulcerations compared to those without ulcerations; similarly in amputations, debridement's V/S AFS. Thus NLR and PLR are useful in demonstrating not only outcomes but also clinical criteria of PVD and CLI presentation by our data. The NLR is mirror of vessel wall inflammation, while PLR pictures pro-thrombotic tendency - owing to higher blood viscosity. Also one documented study highlighted that apart from platelets; the platelet derived micro particles (MP) derived from platelets were associated with formation and progression of arterial thrombi in the context of progressive inflammatory atherosclerosis or secondary to vessel wall injury. The platelets derived MPs causes' procoagulant state leading to its important factor in homeostasis and thrombosis. Elevated PLR might also enhance MP production leading to a state of activated homeostasis: pathological thrombosis / prothrombosis.[25]

CONCLUSION

Higher values of NLR and PLR were found to be having significant associations with amputation versus amputation free survival in our study of 44 cases of PVD/CLI undergoing endovascular management and served as dual prognostic marker as hypothesized. Also NLR and PLR had significant association with Rutherford clinical classification categories and thus elevated NLR and PLR had significant association with clinical presentation criteria as hypothesized and this could be used for pre-endovascular treatment counseling. High NLR was significantly associated with major amputation while a low NLR suggested better limb salvage probability. There was a significant association between PVD and Rutherford clinical classification as well as between NLR and Rutherford's clinical classification.

REFERENCES

1. Swaminathan K, Veerasekar G, Kuppusamy S, Sundaresan M, Velmurugan G, Palaniswami NG. Noncommunicable disease in rural India: Are we seriously underestimating the risk? The Nallampatti noncommunicable disease study. Indian Journal of Endocrinology and Metabolism. 2017;21(1):90-95.
2. Nethan S, Sinha D, Mehrotra R. Non Communicable Disease Risk Factors and their Trends inIndia. Asian Pac J Cancer Prev. 2017;18(7):2005-2010.
3. Siegel KR, Patel SA, Ali MK. Non-communicable diseases in South Asia: contemporary perspectives. British Medical Bulletin. 2014;111(1):31-44.
4. Karakoyun R, Köksoy C, Şener Z, Gündüz U, Karakaş B, Karakoyun M. Comparison of quality of life in patients with peripheral arterial disease caused by atherosclerosis obliterans or Buerger's disease. Cardiovascular Journal of Africa. 2014;25(3):124-129.
5. Beard JD. Chronic lower limb ischemia. Western Journal of Medicine. 2000;173(1):60-63.
6. Dhaliwal G, Mukherjee D. Peripheral arterial disease: Epidemiology, natural history, diagnosis and treatment. The International Journal of Angiology: Official Publication of the International College of Angiology, Inc. 2007;16(2):36-44.
7. Allaqaband S, Kirvaitis R, Jan F, Bajwa T. Endovascular treatment of peripheral vascular disease. Curr Probl Cardiol. 2009.;34(9):359-476.
8. Harsha KJ. Successful Endovascular Neurosurgical Practice in Resource-poor Exclusive Rural Neuro-hospital Setup. Journal of Neurosciences in Rural Practice. 2016;7(Suppl 1):S13-S17.
9. Gary T,Pichler M,et al,Neutrophil-to- Lymphocyte ratio and its Association with critical limb ischemia in PAOD patients. PLoS One 2013;8(2):e56745.
10. Gary T, Pichler M, et al. Platelet to lymphocyte ratio: A novel marker for Critical limb ischemia in peripheral arterial occlusive diseases patients. PLoS One 2013;8(7):e67688.
11. Hammas NW, Dippel EJ. Evidence-based management of peripheral vascular disease. Curr Atheroscler Rep. 2005;7(5):358-63.
12. Aronow WS. Peripheral arterial disease in the elderly. Clinical Interventions in Aging. 2007;2(4):645-654.
13. Alzamora MT, Baena-Díez JM, Sorribes M, Forés R, Toran P, Vicheto M, Pera G, Reina MD, Albaladejo

C, Llussà J, Bundó M, Sancho A, Heras A, Rubiés J, Arenillas JF; PERART study. Peripheral Arterial Disease study (PERART): prevalence and predictive values of asymptomatic peripheral arterial occlusive disease related to cardiovascular morbidity and mortality. BMC Public Health. 2007;7 (3):348.
14. Morris-Stiff G, Ogunbiyi S, Rees J, Davies CJ, Hicks E, Lewis MH. Variations in the anatomical distribution of peripheral vascular disease according to gender. Ann R Coll Surg Engl. 2011;93(4):306-9.
15. Federman DG, Trent JT, Froelich CW, Demirovic J, Kirsner RS. Epidemiology of peripheral vascular disease: a predictor of systemic vascular disease. Ostomy Wound Manage. 1998;44(5):58-62.
16. Davies MG. Criticial Limb Ischemia: Epidemiology. Methodist DeBakey Cardiovascular Journal. 2012;8(4):10-14.
17. Kahraman C, Kahraman NK, Aras B, Coşgun S, Gülcan E. The relationship between neutrophil-to-lymphocyte ratio and albuminuria in type 2 diabetic patients: a pilot study. Archives of Medical Science: AMS. 2016;12(3):571-575.
18. Bhat TM, Afari ME, Garcia LA. Neutrophil lymphocyte ratio in peripheral vascular disease: a review. Expert Rev Cardiovasc Ther. 2016;14(7):871-5.
19. Hardman RL, Jazaeri O, Yi J, Smith M, Gupta R. Overview of Classification Systems in Peripheral Artery Disease. Seminars in Interventional Radiology. 2014;31(4):378-388.
20. Swaminathan A, Vemulapalli S, Patel MR, Jones WS. Lower extremity amputation in peripheral artery disease: improving patient outcomes. Vascular Health and Risk Management. 2014;10(5):417-424.
21. Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, et al. (2006) ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular
22. Iso Y, Soda T, Sato T, Sato R, Kusuyama T, et al. Impact of implanted bone marrow progenitor cell composition on limb salvage after cell implantation in patients with critical limb ischemia. Atherosclerosis 2010;209(2): 167–172.
23. Stabile E, Kinnaird T, la Sala A, Hanson SK, Watkins C, et al. CD8+ T lymphocytes regulate the arteriogenic response to ischemia by infiltrating the site of collateral vessel development and recruiting CD4+ mononuclear cells through the expression of interleukin-16. Circulation 2006;113(4): 118–124.
24. Powell RJ, Goodney P, Mendelsohn FO, Moen EK, Annex BH. Safety and efficacy of patient specific intramuscular injection of HGF plasmid gene therapy on limb perfusion and wound healing in patients with ischemic lower extremity ulceration: results of the HGF-0205 trial. J Vasc Surg 2010;52(5): 1525–1530.
25. Demirkol S, Balta S, Kucuk U, Kucuk HO. The neutrophil lymphocyte ratio may be useful inflammatory indicator before applying other expensive and invasive procedures. Indian Journal of Nephrology. 2014;24(3):65-66.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 21-09-2017; **Published online**: 30-10-2017