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Original Research Article

OBSERVATIONAL STUDY OF CORRELATION OF HBA1C AND NEUTROPHIL LYMPHOCYTE RATIO IN TYPE 2 DIABETES MELLITUS AS A MARKER OF BLOOD SUGAR CONTROL

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ABSTRACT

Background: The Neutrophil-lymphocyte ratio (NLR) values have been used as an assessment tool for level of glycemic control in type 2 diabetic patients. Its high value is a predictor of poor diabetic control. The aim of this study to correlate between NLR, HbA1c and Lipid profile among diabetic population.

Materials and Methods: This present cross-sectional study was conducted on total 440 subjects, out of which 220 type 2 diabetic patients as cases and 220 healthy controls. Venous blood collected in vial with EDTA as anticoagulant. Glycosylated hemoglobin was measured using HbA1c-Direct, Total WBC, neutrophil, lymphocyte levels, Triglyceride, HDL, LDL and Total cholesterol level were assessed. Correlation between two variables was analyzed using Pearson correlation coefficient. A p value < 0.05 was taken as statistically significant.

Results: The mean HbA1C was 4.07 in control and 8.41 in cases and the difference was statistically significant p <0.05. The lipid profile (TC, LDL, TG) was higher in cases as compared to control group & HDL was lower value in cases as compared to control group, which was statistically significant (P<0.001**) in our study. The strong positive correlation between HbA1c and NLR of diabetic patients with a Pearson's coefficient of correlation 0.454 and p <0.05. There no significant correlation with ESR, TC, HDL, LDL, TG with NLR as p value >0.05 which is statistically non-significant and there was moderate positive correlation between HbA1c and NLR in newly and previously diagnosed diabetic patients with p value <0.001.

Conclusion: We concluded that NLR can serve as a marker of long-term diabetic control like glycosylated hemoglobin. NLR can guide the anti-diabetic measures in the resource limited settings and resource limited country like India.

Keywords: HbA1c, NLR, Type 2 Diabetes, Lipid profile, ESR.

INTRODUCTION

The "Diabesity" epidemic (obesity and type 2 diabetes) is likely to be the biggest epidemic in human history. Diabetes has been seriously underrated as a global public health issue and the world can no longer ignore "the rise and rise" of diabetes.[1] The global diabetes prevalence in 2023 is estimated to be 9.3% (529 million people) which denotes such a significant burden it causes on the health.[2]

Type 2 diabetes, the most common form of the disease, may remain undetected for many years and its diagnosis is often made incidentally through an abnormal blood or urine glucose test. It is a multiorgan disease. Macrovascular complications due to chronic hyperglycemia in diabetes are mainly represented by atherosclerotic disease and its

sequelae.[3] Diabetes-related microvascular disease such as retinopathy and nephropathy are major causes of blindness and renal insufficiency.[4] Both type 1 and type 2 diabetes are powerful and independent risk factors for coronary artery disease (CAD), stroke, and peripheral arterial disease.[5] The emerging role of inflammation in diabetes pathophysiology and associated metabolic disorders, has generated increasing interest in targeting inflammation to improve prevention and control of the disease.[6]

After an extensive review of the possible inflammatory mechanisms that drive the metabolic pattern in Type1 Diabetes and Type 2 Diabetes it becomes clear that future research might be focusing on a model of combined suppression for various inflammatory response pathways.[7]

One potential implication of the studies suggesting a relation between inflammation and diabetes is that inflammatory markers may be used to define diabetes risk prediction and thus better target individuals for lifestyle interventions.[7] In another study, authors studied associations of inflammatory markers with the risk of major macrovascular events, microvascular complications and mortality in patients with type 2 diabetes.[8] Concluding that biomarkers of inflammation were associated with an increased risk of macrovascular events and death in analyses adjusted for age, sex, and treatment groups.[9]

Synergistic effect of diabetes and inflammation exists in promoting atherothrombosis and its complications, as well as potential avenues for diagnostic, preventive, and therapeutic benefits in the modulation of inflammatory mechanisms in diabetic atherothrombotic disease.[10]

Total leukocyte count increases significantly in response to infection, inflammation, and certain diseases. Factors affecting leukocyte count in healthy adults include sex, hormonal milieu, genetic inheritance, stress level, diet, nutrition, and lifestyle (e.g. tobacco-induced inflammatory
changes, chronic psychological stress, etc.).[11] Recent findings suggest that elevated leukocyte count within the normal range, but especially neutrophil and monocyte counts, may be a harbinger of increased systemic inflammation and subclinical disease.[12] Remarkably, leukocyte count correlates positively with genuine markers of systemic inflammation like C-reactive protein and interleukin-6.11 The estimated levels of markers like serum ferritin, hs-CRP in type 2
diabetes mellitus was found to be significantly augmented in type 2 diabetes mellitus subjects when compared to control. Suggesting that inflammation plays an important role in the pathogenesis of diabetes and there is strong correlation between inflammation and glycemic control in patient with type 2 diabetes mellitus.[12]

NLR values have been used as an assessment tool of level of glycemic control in type 2 diabetic patients.[13] Its high value is a predictor of poor diabetic control.[13] When compared with other inflammatory biomarkers e.g. ESR and CRP, IL6, Serum Ferritin. The Neutrophil-lymphocyte ratio (NLR) is obtained from routine complete blood count (CBC) test. When correlated with diabetic glycemic control it serves as a cost-effective and easily accessible indicator.

MATERIAL AND METHODS

This present cross-sectional study was conducted on total 440 subjects, out of which 220 type 2 diabetic patients as cases and 220 healthy controls who attended internal medicine wards and OPD, Endocrinology wards and OPD of RNT medical college and associated groups of hospitals, Udaipur during one-year period.

Inclusion Criteria

Cases

- Age > 18 years
- Patients with newly or previously diagnosed type 2 Diabetes Mellitus

Diagnosis of Diabetes

- Symptoms of diabetes plus random blood glucose concentration ≥ 200 mg/dl
- Fasting plasma glucose >126 mg/dl
- 2-hr plasma glucose ≥ 200 mg/dl after oral glucose challenge
- HbA1c ≥ 6.5%

Controls (normoglycemic patients)

- Fasting plasma glucose <100 mg/dl
- 2-hr plasma glucose <140 mg/dl after oral glucose Challenge
- HbA1c <5.6%

Exclusion Criteria

- Type 1 diabetes mellitus
- Severely ill patients unable to give consent
- Established source of infection/Sepsis
- Known case of autoimmune disease/ Chronic kidney disease
- Allergic reactions
- Malignancy
- On chronic drug therapy such as corticosteroids, lithium, heparin, antiepileptic drugs
- Myocardial infarction

• Pregnancy

Methods

2 ml venous blood collected in vial with EDTA as anticoagulant. Glycosylated hemoglobin was measured using HbA1c-Direct, BioSystems BA analyzers.[14]

Neutrophil Lymphocyte Ratio: Specimen volumes required -a minimum of 2 mL whole blood is required for sample analysis. Whole blood diluent (cellpack dcl) for use in hematology analyzers. Total WBC, neutrophil and lymphocyte levels were determined using a flow cytometric method by automated blood c ell counter (SYSMEX XS-1000i-6800).[15]

Lipid Profile Method: Fasting venous blood sample were collected in plane vial. Amount required about 2-4 ml. Analyzed through automated analyzer using principle of Chemiluminescence Technology (Siemens Dimension EXL 200). Obtained assay include Triglyceride, HDL, LDL, Total cholesterol Reference values.[16]

Statistical Analysis

Nominal/categorical variables were summarized as frequency and percentage and were analyzed using Chi square test/Fischer's Exact test as applicable. ANOVA test for more than two group comparison. Correlation between two variables was analyzed using Pearson correlation coefficient. A p value < 0.05 was taken as statistically significant. All statistical analyses were done using Epi info version 7.2.1.0.

RESULTS

This study was conducted on 220 patient of type 2 DM and 220 age sex matched controls. Out of 220 type 2 diabetic cases, 77 (35%) were newly diagnosed type 2 diabetes and 143 (65%) were previously diagnosed case of type 2 DM. The mean HbA1C was 4.07 in control and 8.41 in cases and the difference was statistically significant p <0.05. ESR, marker of inflammation was found to be raised in cases with a mean value of 60.67 mm/hr when compared to control's 10.85 mm/hr and the difference was statistically significant p <0.05. The lipid profile (TC, LDL, TG) was higher in cases as compared to control group & HDL was lower value in cases as compared to control group, which was statistically significant (P<0.001**) in our study. NLR was obtained on dividing absolute neutrophil count by absolute lymphocyte count. The mean NLR among diabetic cases was 3.09, while that in controls was lower 1.38. Difference was statistically significant p <0.05 (table 1).

Most of the cases in newly diagnosed type 2 diabetes were in 31-40 year age group 31 (40.25%). Among previously diagnosed type 2 diabetes maximum cases were in the age group of 61-70 years of age 52 (36.39%) and the difference was statistically significant p <0.05. HbA1C value was found to be high in newly diagnosed type 2 DM (9.93%) as compared to previously diagnosed type 2 DM (7.98%). The comparison was statistically significant p <0.05. The Mean NLR was higher in newly diagnosed DM 3.89 as compared to previously diagnosed 2.89 and the difference was statistically different with p value <0.05 (table 2).

Our study showed that there was a strong positive correlation between HbA1c and NLR of diabetic patients with a Pearson's coefficient of correlation 0.454 and p <0.05. There was no significant correlation with ESR, TC, HDL, LDL, TG with NLR as p value >0.05 which was statistically non-significant and there was moderate positive correlation between HbA1c and NLR in newly and previously diagnosed diabetic patients with p value <0.001 (table 3 & 4)

Table 1: Demographic and laboratory characteristics in cases and control groups

Characteristics		Cases (n=220)	Controls (n=220)	p-value
Sex	Females	109 (49.55%)	106 (48.18%)	>0.05 (NS)
	males	111 (50.45%)	114 (51.82%)	
HbA1c (Mean±SD)		8.41±2.45	4.07±0.60	<0.001 (HS)
ESR (Mean±SD)		60.67±38.19	10.85±4.34	<0.001 (HS)
Total Cholesterol (TC) (Mean±SD)		162.62±53.34	147.53±14.07	<0.001 (HS)
HDL (Mean±SD)		39.04±14.49	47.52±5.26	<0.001 (HS)
LDL (Mean±SD)		94.67±40.51	78.53±4.07	<0.001 (HS)
TG (Mean±SD)		167.10±62.89	114.62±24.38	<0.001 (HS)
NLR (Mean±SD)		3.09±2.55	1.38±0.54	<0.001 (HS)

Table 2: The comparison of age, HbA1c & NLR in Case Study Groups (Newly and Previously Diagnosed Diabetes)

Characteristics	Newly diagnosed diabetes (n=77)	Previously diagnosed diabetes (n=143)	p-value
Age groups (yrs)			
<31	6 (7.79%)	1 (0.69%)	<0.001 (HS)
31-40	31 (40.25%)	9 (6.29%)	
41-50	25 (32.49%)	13 (9.09%)	
51-60	7 (9.09%)	43 (30.06%)	
61-70	3 (3.89%)	52 (36.39%)	
>70	5 (6.49%)	25 (17.48%)	
HbA1c			
Mean±SD	9.93±2.56	7.98±2.15	<0.001 (HS)
NLR			
Mean±SD	3.89±3.86	2.89±1.72	<0.001 (HS)

Table 3: Correlation of NLR with Different Parameters Among Cases

	R	P value
HbA1c	0.454	<0.001 (HS)
ESR	-0.007	>0.05 (NS)
TC	-0.025	>0.05 (NS)

HDL	-0.043	>0.05 (NS)
LDL	0.001	>0.05 (NS)
TG	0.0344	>0.05(NS)

Table 4: Correlation of Hb1Ac with NLR Among Newly and Previously Diagnosed Cases of Diabetes

	R (correlation coefficient)	P value
Newly Diagnosed	0.313	<0.001 (HS)
Previously Diagnosed	0.552	<0.001 (HS)

DISCUSSION

The increase in diabetes incidence can be attributed to changes in dietary pattern, sedentary behavior, and obesity superimposed on the background of genetic and epigenetic susceptibility.[17]

Opportunistic screening for undiagnosed diabetes and prediabetes is recommended. It should include individuals presenting to health care settings for unrelated illness, family members of diabetes patients, antenatal care, dental care, overweight children and adolescents at onset of puberty. Wherever feasible, community screening may be done. All these measures will collaboratively work to reduce burden of diabetes.[18]

Out of the total 220 patients with type 2 diabetes, 111 (50.45%) were males and 109 (49.55%) were females, showing equal prevalence among both sexes. The difference in sex distribution was statistically insignificant with p value >0.05. Our results were consistent with Sarah Wild et al19, Esayas Haregot Hilawe et al,[20] and A Ramachandran et al,[21] with no gender difference between the diabetic cases.

The difference in the age groups of newly diagnosed and previously diagnosed cases of type II diabetics was statistically significant with p value < 0.05. This is consistent with the result published by study conducted by A Ramachandran et al,[21] a National Urban Diabetes Survey among the Indian population which stated that Diabetes and impaired glucose tolerance showed increasing trend with age. Subjects under 40 years of age had a higher prevalence of impaired glucose tolerance than diabetes (12.8% vs 4.6%, p < 0.0001). Similar results were obtained in our studies as newly diagnosed diabetes with impaired fasting glucose had maximum number 31 (40.25%) were in age group less then 40 years.

A national survey of diabetes and impaired glucose tolerance (IGT) conducted in 2000 AD in six major cities of India by C Snehalatha et al,[22] Subjects under 40 years of age had a higher prevalence of impaired glucose tolerance than diabetes (12.8% vs 4.6%, p < 0.0001). Diabetes showed a positive association with age, Similar results were obtained in our study as maximum cases of previously diagnosed diabetes 52 (36.39%) were above 61-70-year age group.

In our study, the mean HbA1c was found to be within normal limit 4.07% in controls and was significantly higher in cases with a mean value of 8.41%. The difference between cases and control was statistically significant with p value <0.001.

Glycosylated hemoglobin value was found to be high in newly diagnosed DM 9.93% as compared to previously diagnosed DM 7.98%. This difference was found to be statistically significant on application of ANOVA test (p<0.001).

This difference was probably due to previously diagnosed type 2 diabetics being on antidiabetic medication while newly diagnosed type 2 diabetics had higher HbA1c due to persistently raised blood glucose levels without any anti diabetic treatment.

David M. Nathan et al,[23] studied in International Expert Committee report on the role of the A1c assay in the diagnosis of diabetes that the results of the A1c-Derived Average Glucose (ADAG) study support the notion of a close relationship between A1c levels and average glucose in diabetes. The A1c assay plays a central role in the clinical management of diabetes.

ESR an acute phase reactant has been utilized as discriminating inflammatory from non-inflammatory disorders. There was a significant difference between ESR levels between diabetic and control population which shows that diabetes is a state of persistent inflammation.

Study conducted by Mubin Mustafa Kiyani et al,[24] showed that the relationship between erythrocyte sedimentation rate (ESR) in diabetic (DM) and non-diabetic patients of cardiovascular diseases (CVD). Pearson correlation between ESR of CVD without DM and ESR of CVD with DM, and they determined that there is a weak relationship between these two variables. Value of Pearson ‘r' between these two variables is 0.160.

The relationship between the erythrocyte sedimentation rate (ESR), glycosylated hemoglobin, and the concentrations of plasma proteins was investigated in 34 outpatients with diabetes mellitus by AN Elias et al.[25] The ESR was found to be significantly elevated, the degree of elevation correlating with the serum globulin concentration, the albumin-globulin ratio, the serum fibrinogen concentration and the percent glycosylated hemoglobin (HbA1c). The data indicates that the ESR in diabetic patient may be elevated in the absence of overt infection. Our results were in accordance to above studies and showed a positive correlation between raised ESR in diabetes to normal range in controls.

Individuals with DM may have several forms of dyslipidaemia because of the additive cardiovascular risk of hyperglycemia and hyperlipidemia, lipid

abnormalities should be assessed aggressively and treated as part of comprehensive diabetes care. The most common pattern of dyslipidaemia is hypertriglyceridemia and reduced high density lipoprotein (HDL) cholesterol levels.

Due to oxidative modification and glycation of the HDL protein as well as the transformation of the HDL proteome into proinflammatory protein HDL properties are compromised in patients with diabetes mellitus (DM). Numerous studies confirm that the ability of HDL to suppress inflammatory signals is significantly reduced in this group of patients.[26]

In a study of lipid profile in diabetic patients by Owei I et al,[27] analyzed data from 335 healthy adults (184 black, 151 white). Fasting plasma glucose correlated positively with triglycerides and LDL cholesterol levels and inversely with HDL cholesterol levels (P = 0.006, <0.0001); insulin sensitivity correlated positively with HDL cholesterol and inversely with triglyceride levels (P <0.0001), and insulin secretion correlated positively with triglycerides (P=0.01) and inversely with HDL cholesterol (P <0.0001). This is consistent with our study that increased level are there of total cholesterol, TG and LDL while decreased value of HDL among diabetic population.

In a study done in rural population of Bangladesh on 2293 adults Bishwajit Bhowmik et al,[28] showed significant linear trends were observed for high T-Chol, high TG and low HDL with increasing glucose intolerance. Type 2 DM was significantly associated with high Total cholesterol, high TG and low HDL these results were also consistent with our studies.

In a study conducted by Hussain M et al,[13] concluded that increased NLR level is associated with elevated HbA1c and poor glycemic control in patients of type 2 diabetes mellitus. In another study done by Shiny et al,[29] subjects with DM showed a significantly higher NLR (2.2±1.12) compared with IGT subjects (1.82±0.63), who in turn had a higher ratio than NGT subjects (1.5±0.41) (P<0.01). Pearson correlation analysis showed a significant positive correlation of NLR with glycated hemoglobin (r=0.411), fasting plasma glucose (r=0.378), and HOMA-IR (r=0.233) (P<0.001).

Our results are consistent with study conducted by C Mertoglu et al[30] in which, NLR was significantly higher in Group with IGT (1.60), Group with newly diagnosed diabetic (1.58) and Group with previously diagnosed diabetes (2.07) compared to normoglycemic patients (1.37). They concluded that inflammation marker NLR significantly increases in the diabetic patients.

The results of the current study are in agreement with the study conducted by Meiqin Lou et al,[31] found the NLR values of the diabetic patients were significantly higher than those of the healthy control (P < 0.001), and the NLR values of the patients with insulin resistance was higher than those without insulin resistance (P < 0.001).

Pearson correlation coefficient for HbA1C with NLR was 0.454. There was a positive correlation between HbA1c and NLR (p<0.001). i.e. as HbA1c increased, NLR increased significantly. Devamsh G. N et al,[32] studied the relationship between NLR and glycemic control in type 2 diabetes patients. NLR had a positive correlation with HbA1c and was found to be an independent predictor of poor glycemic control in patients with type 2 diabetes mellitus.

Akin et al,[33] studied A total of 278 Type 2 diabetic patients. The patients were divided into two groups: the good glycaemic control group (HbA1c ≤7.5%) and the poor glycaemic control group (HbA1c >7.5%). NLR was compared between the diabetic groups. In addition, NLR was compared with diabetic patients and control group. The NLR was statistically and significantly higher in the poor glycaemic control group compared to the good glycaemic control group. In addition, NLR was significantly higher in the patients than in the control group.

Our study also observed that there was no correlation between variation in total cholesterol and LDL with glycemic control in diabetic cases with HbA1c levels with p value >0.05. Liu et al,[34] studied three hundred thirty-five patients with Type 2 DM. Univariate analyses identified that NLR was positively correlated with age, glycosylated hemoglobin (HbA1c), triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL). However, our results did not agree to the same.

CONCLUSION

We concluded that NLR can serve as a marker of long-term diabetic control like glycosylated hemoglobin. NLR can guide the anti-diabetic measures in the resource limited settings and resource limited country like India. NLR may be useful as an easily measurable, invasive, available, and cost- effective parameter for the follow-up of diabetic patients.

REFERENCES

1. Zimmet, Paul Z. Diabetes and its drivers: the largest epidemic in human history?. Clinical diabetes and endocrinology,2017;3(1):18.
2. Saeedi, P., Petersohn, I., Salpea, P., Malanda, B., Karuranga, S., Unwin, N., Colagiuri, S., Guariguata, L., Motala, A. A., Ogurtsova, K., Shaw, J. E., Bright, D., Williams, R., & IDF Diabetes Atlas Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. Diabetes research and clinical practice,2019; 157:107843.
3. Aronson D. Hyperglycemia and the pathobiology of diabetic complications. Advances in cardiology,2008; 45:1-16.
4. Barot M, Gokulgandhi MR, Patel S, Mitra AK. Microvascular complications and diabetic retinopathy: recent advances and future implications. Future Med Chem. 2013 ;5(3):301-14.
5. Paneni F, Beckman JA, Creager MA, Cosentino F. Diabetes and vascular disease: pathophysiology, clinical

consequences, and medical therapy: part I. Eur Heart J. 2013 ;34(31):2436-43.
6. Tsalamandris S, Antonopoulos AS, Oikonomou E, Papamikroulis GA, Vogiatzi G, Papaioannou S, Deftereos S, Tousoulis D. The Role of Inflammation in Diabetes: Current Concepts and Future Perspectives. Eur Cardiol. 2019 ;14(1):50-59.
7. Wang X, Bao W, Liu J, Ouyang YY, Wang D, Rong S, Xiao X, Shan ZL, Zhang Y, Yao P, Liu LG. Inflammatory markers and risk of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2013 Jan;36(1):166-75.
8. Lowe G, Woodward M, Hillis G, Rumley A, Li Q, Harrap S, Marre M, Hamet P, Patel A, Poulter N, Chalmers J. Circulating inflammatory markers and the risk of vascular complications and mortality in people with type 2 diabetes and cardiovascular disease or risk factors: the ADVANCE study. Diabetes. 2014 Mar;63(3):1115-23.
9. Tandon, N., Ali, M. K., & Narayan, K. M. Pharmacologic prevention of microvascular and macrovascular complications in diabetes mellitus: implications of the results of recent clinical trials in type 2 diabetes. American journal of cardiovascular drugs: drugs, devices, and other interventions,2012; 12(1) 7-22.
10. Biondi-Zoccai GG, Abbate A, Liuzzo G, Biasucci LM. Atherothrombosis, inflammation, and diabetes. J Am Coll Cardiol. 2003 Apr 2;41(7):1071-7.
11. Chmielewski PP, Strzelec B. Elevated leukocyte count as a harbinger of systemic inflammation, disease progression, and poor prognosis: a review. Folia Morphol (Warsz). 2018;77(2):171-178.
12. Elimam H, Abdulla AM, Taha IM. Inflammatory markers and control of type 2 diabetes mellitus. Diabetes Metab Syndr. 2019;13(1):800-04.
13. Hussain M, Babar MZM, Akhtar L, Hussain MS. Neutrophil lymphocyte ratio (NLR): A well assessment tool of glycemic control in type 2 diabetic patients. Pak J Med Sci. 2017 ;33(6):1366-70.
14. Powers AC. Diabetes Mellitus. In: Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson L,editors. Harrison's principles of internal medicine.20th ed. McGraw-Hill;2005. p. 2850.
15. Moosazadeh, M., Maleki, I., Alizadeh-Navaei, R., Kheradmand, M., Hedayatizadeh-Omran, A., Shamshirian, A., & Barzegar, A. Normal values of neutrophil-to-lymphocyte ratio, lymphocyte-to- monocyte ratio and platelet-to-lymphocyte ratio among Iranian population: Results of Tabari cohort. Caspian journal of internal medicine,2019;10(3):320-25.
16. Grundy, S. M., Cleeman, J. I., Daniels, S. R., Donato, K. A., Eckel, R. H., Franklin, B. A., Gordon, D. J., Krauss, R. M., Savage, P. J., Smith, S. C., Jr, Spertus, J. A., Costa, F., American Heart Association, & National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation,2005; 112(17):2735- 52.
17. Hu FB Globalization of diabetes: the role of diet, lifestyle, and genes. Diabetes Care 2011; 34:1249-57.
18. Chawla R, Madhu SV, Makkar BM, Ghosh S, Saboo B, Ka lra S; RSSDI-ESI Consensus Group. RSSDI-ESI Clinical Practice Recommendations for the Management of Type 2 Diabetes Mellitus 2020. Indian J Endocrinol Metab. 2020 ;24(1):1-122.
19. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004 ;27(5):1047-53.
20. Hilawe EH, Yatsuya H, Kawaguchi L, Aoyama A. Differences by sex in the prevalence of diabetes mellitus, impaired fasting glycaemia and impaired glucose tolerance in sub-Saharan Africa: a systematic review and meta-analysis. Bull World Health Organ. 2013;91(9):671-682D.
21. Ramachandran A, Snehalatha C, Kapur A, Vijay V, Mohan V, Das AK, Rao PV, Yajnik CS, Prasanna Kumar KM, Nair JD; Diabetes Epidemiology Study Group in India (DESI). High prevalence of diabetes and impaired glucose tolerance in India: National Urban Diabetes Survey. Diabetologia. 2001 ;44(9):1094-101.
22. Snehalatha C, Ramchandran A, Kapur A, Vijay V. Age-specific prevalence and risk associations for impaired glucose tolerance in urban southern Indian population. J Assoc Physicians India. 2003; 51:766-769.
23. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care. 2009 Jul;32(7):1327-34.
24. Kiyani, M., Jahan, S., Kiyani, S., Rehman, H., Khan, L., & Iqbal, U. (2019). Erythrocyte sedimentation rate in diabetic and non- diabetic patients of cardiovascular disease. Jurnal Teknologi Laboratorium, 8(1), 18-22.
25. La Moreaux B. Correlation of Erythrocyte Sedimentation Rate with Glycohemoglobin Values and Other Patient Factors [abstract]. Arthritis Rheumatol. 2016; 68 (suppl 10). https://acrabstracts.org/abstract/correlation-of-erythrocyte-sedimentation-rate-with-glycohemoglobin-values-and-other-patient-factors/. Accessed 25, 2021.
26. Femlak M, Gluba-Brzózka A, Ciałkowska-Rysz A, Rysz J. The role and function of HDL in patients with diabetes mellitus and the related cardiovascular risk. Lipids Health Dis. 2017;16(1):207. Published 2017;30.
27. Owei I, Umekwe N, Wan J, Dagogo-Jack S. Plasma lipid levels predict dysglycemia in a biracial cohort of nondiabetic subjects: Potential mechanisms. Exp Biol Med (Maywood). 2016;241(17):1961-67.
28. Bhowmik B, Siddiquee T, Mujumder A, Afsana F, Ahmed T, Mdala IA, do V Moreira NC, Khan AKA, Hussain A, Holmboe- Ottesen G, Omsland TK. Serum Lipid Profile and Its Association with Diabetes and Prediabetes in a Rural Bangladeshi Population. Int J Environ Res Public Health. 2018 :6;15(9):1944.
29. Shiny A, Bibin YS, Shanthirani CS, Regin BS, Anjana RM, Balasubramanyam M, Jebarani S, Mohan V. Association of neutrophil-lymphocyte ratio with glucose intolerance: an indicator of systemic inflammation in patients with type 2 diabetes. Diabetes Technol Ther. 2014;16(8):524-30.
30. Mertoglu C, Gunay M. Neutrophil-Lymphocyte ratio and Platelet- Lymphocyte ratio as useful predictive markers of prediabetes and diabetes mellitus. Diabetes Metab Syndr. 2017;11 Suppl 1: S127- S131.
31. Lou M, Luo P, Tang R, Peng Y, Yu S, Huang W, He L. Relationship between neutrophil-lymphocyte ratio and insulin resistance in newly diagnosed type 2 diabetes mellitus patients. BMC Endocr Disord. 2015; 2:15:9.
32. N., Devamsh G. et al. Study of neutrophil lymphocyte ratio in patients with type 2 diabetes mellitus and its correlation with glycemic control. International Journal of Advances in Medicine,2019;6(5):1637-41.
33. Seydahmet Akin, Zeki Aydin, Guven Yilmaz, Mehmet Aliustaoglu, Ozcan Keskin. Evaluation of the relationship between glycaemic regulation parameters and neutrophil-to-lymphocyte ratio in type 2 diabetic patient. EMJ Diabet 2019;7[1]:91-96.
34. Liu N, Sheng J, Pan T, Wang Y. Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio are Associated with Lower Extremity Vascular Lesions in Chinese Patients with Type 2 Diabetes. Clin Lab. 2019:1;65(3).