Current Science International
Volume: 12 | Issue: 01| Jan. - March| 2023

EISSN:2706-7920 ISSN: 2077-4435
DOI: 10.36632/csi/2023.12.1.8
Journal homepage: www.curresweb.com
Pages: 68-76

Monocytes to High-Density lipoprotein Cholesterol Ratio as a New Marker for Diabetic Nephropathy and Retinopathy

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Received: 09 Feb. 2023 **Accepted:** 12 Mar. 2023 **Published:** 20 Mar. 2023

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a major health problem and its prevalence is increasing worldwide which results in high morbidity and mortality due to its wide spectrum of complications. Both diabetic nephropathy (DN) and diabetic retinopathy (DR) are serious microvascular complications and have been considered the major cause of blindness and end-stage renal failure. **Objective:** our study was conducted to assess the Monocytes to High-Density lipoprotein Cholesterol ratio (MHR) as a New Marker for DN and DR. **Patients and methods:** the study was conducted on 100 subjects 50 were healthy control and 50 had a diagnosis of T2DM according to American Diabetes Association Criteria (ADAC). Data were collected including, demographic, clinical, and laboratory data. Statistical analysis was carried out for all collected data using IBM SPSS. Statistical significance was determined at a p -value<0.05. **Results:** MHR was normal in the healthy control group with a median of 7.23 while it was high in patients with DN and DR with a median of (16.8) - (18.6) respectively. These patients had a longer duration of DM, higher lipid profile values, and bad control of DM which was assessed by HbA1c, associated metabolic syndrome, micro, and macro albuminuria. **Conclusion:** our current study suggests that MHR is associated with the presence of DN and DR so it can be used as a new marker for the progression and development of DN and DR.

Keywords: Type 2 diabetes mellitus, chronic kidney diseases.

1. Introduction

Diabetes mellitus is a global health burden. Its mortality and morbidity are increasing in the last few years (Pan *et al.,* 2017).

Globally, the number of people with diabetes mellitus has doubled in the past three decades. Also, DM is the ninth major cause of death all over the world. About 1 in every 11 adults now have DM, 90% of whom have type 2 DM (Naghavi *et al.,* 2015).

International Diabetes Federation (IDF) has stated that diabetes mellitus is a major health problem worldwide. IDF listed Egypt among the world's top 10 countries in the number of patients with diabetes the IDF estimated that 7.5 million individuals have diabetes and around 2.2 million have pre-diabetes in Egypt it is expected the number will rise to 13.1 million by 2035 (Cho *et al.,* 2018).

Diabetic microvascular complications which mainly occurred as a result of hyperglycemia can progress to severe impairment in several organs. Diabetic nephropathy and diabetic retinopathy are the most common microvascular complications of hyperglycemia (Nentwich *et al.,* 2015).

Thus, clinicians and researchers need to understand the pathogenesis of these complications. Diabetic nephropathy remains one of the most frequent complications of both types of diabetes. DM is the leading cause of end-stage renal disease ESRD, accounting for approximately 50% of cases in the developed world. It is a major cause of morbidity and mortality in diabetic patients due to the

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association between the development of ESRD and cardiovascular diseases, especially in patients with T2DM (Liu *et al.,* 2018).

Diabetic retinopathy is the leading cause of blindness among working-aged adults around the world. DR can develop in a patient with type 1 or 2 diabetes with a long history of diabetes, poor glycemic, and blood pressure control are strongly associated with DR. (Yau *et al.,* 2012).
Diabetic retinopathy is a progressive condition with microvascular alterations that lead to retinal ischemia, increased retinal permeability, retinal neovascularization, and macular edema.
(Engerman *et al.,* 1989).

Inflammatory response plays an important role in the development and progression of DN and DR. There is an association between chronic inflammation DN, and DR. Elevated CRP levels were observed in patients with DR, as compared to DM patients without DR. Besides, various inflammatory cytokines, such as interleukin-1, -6, and -8 were also considered to be highly associated with the pathogenesis of DN. It was found that monocyte contributes to local and systemic inflammation by producing inflammatory cytokines. These cytokines have been demonstrated to take part in the pathogenesis of vascular inflammation in diabetic patients (Shi and Pamer, 2011).

High-density lipoprotein cholesterol HDL-C also protects endothelial functions and has antioxidant efficacy so a decrease in its level plays a risk factor in the inflammatory process (Assmann and Gotto*,* 2014).

In the last years, MHR is a novel indicator of systemic inflammatory response in various diseases and was considered an independent predictor of major, morbidity, mortality, and long-term survival in many clinical settings. In addition, an increase in MHR was found to be associated with micro-albuminuria due to increase inflammation and endothelial dysfunction (Karatas *et al.,* 2018).

So many studies have suggested that (MHR) may be a predictor of the development and progression of DN and DR. (Cakir *et al.,* 2020).

The aim of the work was to assess the monocytes to high-density lipoprotein ratio as a new marker for diabetic nephropathy and retinopathy.

2. Patients and Methods

Study Design: Observational cross-sectional study.
Study population: This cross-sectional study includes 100 subjects divided into 2 groups:
Group 1 includes 50 healthy control subjects.
Group 2 includes 50 patients with T2DM our patients were 52% males, and 48% females whose ages ranged between 45 and 78 years. Group 2 was divided into two subgroups:
Group 2A includes 25 patients with type 2 diabetes with diabetic nephropathy and non-proliferative diabetic retinopathy.
Group 2B includes 25 patients with type 2 diabetes with diabetic nephropathy and proliferative diabetic retinopathy.

The patients were recruited from, Internal Medicine Department and Tanta university hospitals in the period between May 2021 to May 2022.

Ethical consideration:

Permission was obtained from Research Ethics Committee as a part of the Quality Assurance Unit in the Faculty of Medicine at Tanta University to conduct this study and to use the facilities in the hospital. Informed written consent was obtained from all patients.

Provision of privacy*:*

Privacy of all data was guaranteed as the following: There was a code number for each patient, so the data of patients were strictly confidential.
Inclusion criteria: Fifty Patients with type 2 diabetes meeting 2017 American Diabetes Association criteria were selected from Internal Medicine Department at Tanta University Hospitals.
Exclusion criteria: Patient under the age of 18. Blood disease that affects monocytes. Active urinary infection. Other causes of proteinuria as Nephrotic syndrome or liver disease. Coincident retinal pathology as retinal vein occlusion, age-related macular degeneration, and choroidal neovascularization.

Possible Hazards during the research: The slight risks of bleeding or infection during blood sampling for investigations, it was avoided by good compressing or by using sterile techniques. No other hazards are expected during the period of research. There was safe disposal of waste products e.g., needles…etc. Any unexpected risks that appeared during the research were cleared to participants and the ethical committee on time.

Methods:

Full history taking: Including age, sex, smoking, duration of DM, history of receiving medication for chronic diseases, and presence of any known kidney disease.

Complete clinical examination: Measurement of systolic and diastolic blood pressure. Chest, cardiac, and abdominal examination to exclude subjects with any abnormal findings.

Examination of the eye especially the posterior segment (fundoscopy).

Laboratory investigation: Complete blood count. ESR and CRP. Fasting, 2hpp, and HbA1C. Blood urea and serum creatinine. Urine analysis and test for albuminuria. Urinary Albumin creatinine ratio. Lipid profile (Triglyceride, cholesterol, LDL, and HDL). ANA. HCV and HBV.

Blood sampling and processing: Under quality control and safety procedure for sample collection, an 8 ml venous blood sample was collected in plain vacutainer tubes. 2 ml was added to EDTA for CBC assay. Serum was separated from the other 6 ml blood for all specimens using centrifugation at 3000 rpm for 15 min. serum sample for assayed for urea, creatinine, lipid profile, and CRP.

Renal function test: Blood urea and serum creatinine are automated by (Au 480-Beckman colter). The lipid profile was carried out by colorimetric techniques. CBC automated by ERMA PCE-210N cell counter. CRP uses a rapid latex agglutination test for the qualitative screening and semi-quantitative determination of CRP in serum. ESR: expresses in mm per hour the rate at which red blood cells settle when anti-coagulated blood is allowed to stand in a narrow tube. It is measured by the height of the column of clear plasma at the end of one hour.

MHR was a result of the number of monocytes in CBC divided on the level of HDL.

Statistical analysis of the data

Data were analyzed using the IBM® SPSS statistical software, version 21. We used the one-sample Kolmogorov—Smirnov test to check the normality of the data some data were parametric and others were non-parametric. Numerical data were presented as mean and standard deviation (SD) and categorical data were presented as numbers and percentages. Chi-squared test was used for comparing the qualitative data. One Way of Anova test (ANOVA) test was used to compare the means in different groups if the data were parametric. While Kruskal-Wallis test was used also to compare the means in different groups if the data were non-parametric. Significance between groups was done using Post Hoc Test (Tukey HSD test) linear correlation analysis was done by spearman coefficient correlation and used to test the positive or negative associations between different variables. For the risk estimated, Linear regression was used to detect the predictor variables Receiver operating characteristic (ROC) curve analysis was done to detect the sensitivity and specificity of the studied marker. The level of significance was adopted at $p<0.05$. The ROC (receiver operating characteristic) curve: The ROC curve is a graphical representation of the interaction between sensitivity and specificity for a diagnostic test at various cutoff points. The left upper corner of the curve is a good diagnostic test. Sensitivity and specificity are both 100% at this point. The point of the curve closest to the upper left corner provides the highest test potential and minimizes the sum of incorrect diagnoses. The area below a curve is the overall accuracy of the test; the bigger the zone, the better the results. The curve nearest to the upper left corner is more sensitive and specific, which means that both curves are more accurate.

3. Results

There was a significant difference (increase) between patients with T2DM and our normal control subjects in Fasting blood glucose, 2hpp HbA1C, ACR, Monocytes, TG, Cholesterol, ESR, CRP, and MHR. While there was a significant difference (decrease) between patients with T2DM and our normal control subjects in HDL level. On the other hand, there was an insignificant difference

between patients with T2DM and our normal control subjects in Age, Sex, Blood pressure, and Platelets (Table 1).

Table 1: Comparison between the two studied groups according to: FBG,2 HHP, HbA1C, Monocytes, ESR, CRP, HDL, LDL, CHOLESTROL, TRIGLYCERIDES, ACR, MHR, Blood urea and serum Creatinine.

Parameter	Mean ± SD Median	Group I	Group (2A)	Group (2B)	H(P value)
FBG (mg/dL)	Mean ± SD	85.76 ±15.25	137.72 ± 24.21	163.42 ± 19.31	60.24(0.014)
	Median	86	132.0	165.0	
2hpp (mg/dL)	Mean ± SD	154.70 ± 13.62	275.62 ± 36.41	287.51 ± 30.46	180.5(0.001)
	Median	155.0	285.0	290.0	
HbA1C %	Mean ± SD.	4.65 ± 0.44	9.95 ± 1.94	10.75 ± 1.04	53.43(0.001)
	Median	4.7	9.5	10.5	
Monocytes (cell/mm)	Mean ± SD.	389.4 ± 58.01	610.3 ± 128.2	648.2 ± 68.5	96.33(0.001)
	Median	375.0	650.0	673.0	
ESR1hour mm\h	Mean ± SD.	15.74 ± 7.8	37.10 ± 11.16	37.00 ± 16.16	44.80(0.001)
	Median	15.0	40.0	35.0	
ESR2hour mm\h	Mean ± SD	33.20 ± 15.36	74.60 ± 21.16	74.20 ± 26.16	53.43(0.001)
	Median	30.0	75.0	75.0	
CRP mg/l	Mean ± SD.	9.16 ± 5.44	19.96 ± 24.4	15.18 ± 18.14	1.92 (0.05)
	Median	8.0	12.0	12.0	
TG (mg/dL)	Mean ± SD.	149.4 ± 23.2	185.8 ± 34.3	185.4 ± 24.44	22.25(0.001)
	Median	135.0	190.0	180.0	
HDL (mg/dL)	Mean ± SD.	50.68 + 6.49	37.6 + 4.5	38.4 + 4.9	62.35(0.001)
	Median	50.5	38.0	38.0	
LDL	Mean ± SD.	94.52 +10.85	119.48 ± 16.61	116.48 ± 19.61	30.86(0.001)
	Median	95.0	122.0	117.0	
Cholesterol (mg/dL)	Mean ± SD	210.27 ± 24.8	232.66 ± 27.2	229.66 ± 24.2	8.32(0.01)
	Median	145.0	240.0	231.0	
Urea (mg/dL)	Mean ± SD	34.35± 4.25	110.02 ± 31.12	113.40 ±30.12	49.21(0.001)
	Median	35.0	103.0	101.0	
Creatinine (mg/dL)	Mean ± SD	0.77 ± 0.15	2.21 + 0.18	2.80 + 0.76	126.25(0.001)
	Median	0.76	2.10	2.40	
ACR (mg/g)	Mean ± SD				
	Median				
MHR	Mean ± SD	7.7 ± 1.5	16.41 ± 4.14	17.28 ± 3.14	126.25 (0.01)
	Median	7.23	17.6	16.8	

FBG: Fasting blood glucose 2HPP: 2Hour post prandial ESR: Erythrocyte sedimentation rate CRP:C Reactive protein TG: Triglycerides HDL: High- density lipoprotein LDL: Low -density lipoprotein ACR: Albumin creatinine ratio MHR: Monocyte to High- density lipoprotein cholesterol ratio.

The DN and proliferative diabetic retinopathy were positively correlated with age, HBA1C, ESR, WBCs, monocytes, urea, creatinine, CRP, triglycerides, cholesterol, LDL, and MHR. Also, the DN and proliferative diabetic retinopathy were negatively correlated with hemoglobin, ACR, and HDL (Table 2).

The multivariate analysis revealed that WBCs count, monocytes, urea, creatinine, and MHR were significantly associated with diabetic nephropathy and proliferative diabetic retinopathy (Table 3).

Table 2: Spearman correlation of the presence of diabetic nephropathy and proliferative diabetic retinopathy with other parameters

Cases	Proliferative diabetic retinopathy	
	r	P-value
Age	0.69	0.001*
HbA1C	0.84	0.001*
ESR	0.65	0.001*
CRP	0.16	0.11
Hb	-0.69	0.001*
WBCs	0.40	0.001*
Platelets	-0.045	0.56
Monocytes	0.77	0.001*
Urea	0.67	0.001*
Creatinine	0.88	0.001*
ACR	- 0.55	0.001*
CRP	0.74	0.005*
Triglycerides	0.55	0.001*
Cholesterol	0.58	0.001*
HDL	-0.60	0.002*
LDL	0.33	0.001*
MHR	0.79	0.001*

Table 3: Logistic regression for predictor factors affecting the diabetic nephropathy and proliferative diabetic retinopathy among the studied cases.

	Standardized Coefficients		t	Sig.	95% Confidence Interval	
	Beta	Std error			Lower Bound	Upper Bound
Age	-0.046-	0.070	0.428	0.513	0.833	1.095
Sex	-0.317-	0.984	0.104	0.747	0.106	5.010
WBCs	0.001	0.000	5.078	0.024*	1.000	1.001
Platelets	0.010	0.034	0.081	0.776	0.944	1.080
Monocytes	0.018	0.038	2.213	0.044*	1.944	3.097
CRP	-0.271-	0.239	1.292	0.256	0.478	1.217
HBA1C	0.007	0.025	0.083	0.773	0.960	1.057
Urea	-2.790-	1.063	6.885	0.009*	0.008	0.494
Creatinine	0.006	0.003	4.307	0.038*	1.000	1.012
ACR	-0.017-	0.023	0.523	0.469	0.940	1.029
Triglycerides	0.024	0.041	0.348	0.555	0.946	1.110
Cholesterol	-0.300-	0.597	0.253	0.615	0.230	2.387
HDL	0.016	0.030	4.279	0.0597	0.958	1.077
LDL	-0.737-	1.368	0.290	0.590	0.033	6.985
MHR	-0.046-	0.070	3.428	0.013*	1.833	2.095
CRP	-0.317-	0.984	0.104	0.747	0.106	5.010

4. Discussion

Diabetes mellitus represents one of the most important health problems worldwide. Over the last years, the global prevalence of T2DM has reached epidemic proportions by the global rise in the prevalence of obesity and unhealthy lifestyles (Guariguata *et al.,* 2014).

Diabetic nephropathy is one of the most common complications of diabetes. The prevalence of DN is increasing steeply along with the diabetes epidemic. Approximately one-third to half of the patients with DM develop renal manifestations (Zhang *et al.,* 2020).

During this prolonged asymptomatic period, unmanaged elevated blood glucose leads to a serious and irreversible development of micro- and macrovascular complications include neuropathy, nephropathy, retinopathy, coronary artery disease, stroke, and peripheral vascular disease (Orban *et al.,* 2017).

The objective of this study was to assess the monocytes to high-density lipoprotein ratio as a new marker for diabetic nephropathy and retinopathy.

In the current study regarding to HbA1C there was a statistically significant difference between all studied groups as regards HbA1c (p-value ≤ 0.05). By using a post hoc test there was a significant decrease between (group 1 & group 2A) and (group 1 & group 2B). However, there was no significant difference between (group 2A & group 2B.

This finding is in line with a systematic review conducted in Oman. Obtained by Alrawahi *et al.* (2012) reported that the incidence of diabetic nephropathy was 42.5% and the significant risk factors associated with it include long duration of diabetes, family history of diabetic nephropathy, and poor glycemic control (high HbA1c).

Niveditha *et al.* (2013) A study was done to find out the relation between the level of HbA1c with diabetic retinopathy. An observational clinical study where 50 patients with DR were included. HbA1c of these patients was measured and the correlation between these values with the severity of retinopathy was assessed. Among 50 patients, 31 were males and 19 were females. The mean age of patients was 62 years. The mean duration of diabetes mellitus was 6.9 years. 64.3% with mild NPDR, 78.2% with moderate NPDR, 87.5% with severe NPDR, and 100% of patients with PDR had HbA1c under poor control. Glycosylated hemoglobin showed an increasing trend as the severity of diabetic retinopathy increased.

Regarding albumin creatinine ratio in the studied cases was high in all the studied cases with a mean value of 1126.10 ± 570.2 which is a good indicator of the presence and progression of DN and DR. Moreover, there was a statistically significant difference between all studied groups as regards albumin/ creatinine ratio (p-value ≤ 0.05. By using a post hoc test there was a significant decrease between (group 1 & group 2A) and (group 1 & group 2B). However, there was no significant difference between (group 2A & group 2B).

The same situation was in India which was proved by Pathania *et al.* (2013) who examined 179 patients with T2DM. Out of 179 participants, 7 (3.91%) participants were having urinary albumin concentration in the macro-albuminuria range and 50 (27.93%) participants were in the micro-albuminuria range and 122 (68.16%) were found to be in the normal range according to the ACR ratio. Out of 179 participants, 57 participants (31.84%) were found to have nephropathy.

Similarly (Romero-Aroca *et al.,* 2018) a study was done on 15,811 T2DM patients. It was conducted in Spain a prospective Ten-year follow-up population-based study determined urine albumin to creatinine ratio. Results of the annual incidence of DR were (7.06%-8.92%) and diabetic macular edema (DME) was (2%-2.49%). Renal study results were as follows UACR>30mg\g had an annual incidence of (6.97%-7.09%), 1.584-3.732). The UACR has a better association with diabetic retinopathy than the eGFR, although both are important risk factors for diabetic retinopathy.

The present study revealed that monocyte number among T2DM patients was a statistically significant increase between all studied groups (p- value ≤ 0.05) with a median value (650) in patients with DN.

This coincides with a Japanese study by Shikata and Makino, (2013) who measured the level of monocytes in 130 patients diagnosed with T2DM 74 of them were complicated with DN. The results stated that monocyte count showed a significant increase between the groups.

Also, agreed with Xu *et al.* (2017) in China a study on a total of 557 newly diagnosed T2DM patients was recruited, including 397 T2DM patients without complications as well as 160 T2DM patients complicated with DN and DR who stated that monocyte count showed a significant increase between the groups.

Concerning the HDL level, it was low in all the studied diabetic cases with mean values of (37.6) there was a statistically significant difference between all studied groups as regards HDL.

This result agrees with Hirano (2014) a Japanese study stated that patients with advanced DN and DR have diminished levels of HDL.

In contrast to our present study, Ulu *et al.* (2016) a study that include 58 patients diagnosed with T2DM 24 of them had diabetic nephropathy and retinopathy. The control group was composed of 52 age- and sex-matched healthy subjects who stated that HDL, showed no significant difference between the groups.

HDL is diminished because of several mechanisms. First, patients who have T2DM often have decreased levels of apolipoproteins AI and AII, the main components of HDL. Furthermore, in diabetic patients, the activity of lecithin–cholesterol acyltransferase, the enzyme important for the esterification of free cholesterol in HDL, is impaired. On the other hand, the activity of cholesterol ester transfer protein (CETP), which supports the transfer of cholesterol esters from HDL to triglyceride-rich lipoproteins, is increased. All these processes are responsible for the decreased serum level of HDL (Mikolasevic *et al.,* 2017).

MHR is a marker used for assessing inflammation. MHR has been used widely to evaluate patients with different illnesses. MHR is a marker that is related to immune pathways. Increasing monocytes and decreasing HDL can predict inflammation and affection of the immune system, so high MHR, proteinuria, and retinopathy suggest that they have an immune inflammatory basis. (Onalan *et al.,* 2019).

In the present study, we found a significant elevation of MHR in the patient group compared with the healthy control group and we found a positive correlation between MHR with CRP, ESR, HbA1c, and ACR with the progression of diabetic nephropathy and retinopathy.

Also, agreed with (Onalan *et al.,* 2019) a study that includes 262 diabetic patients, of which 60 had diabetic nephropathy, and a control group comprised of 50 healthy individuals. The study determined the MHR respectively as (11.9±5.5 and 8.4±2.9) for the diabetic group and the healthy group. There was a statistically significant difference between the two groups in terms of MHR, with a positive correlation between diabetes and MHR. Moreover, glucose, HDL, and triglyceride levels were different between the two groups.

The same was proven in Turkey by Erdem and Kaya (2021) who examined a total of 118 T2DM patients, 60 of whom had diabetic retinopathy, and 58 age- and sex-matched healthy controls were included in a cross-sectional study. MHR was calculated by blood sampling after a complete ophthalmologic examination on all subjects. Results MHR was higher in T2DM patients with DR compared to both the control group and without DR ($p=0.018$). There was a significant positive correlation between MHR and DR ($r=0.256$ $p=0.004$). Additionally, MHR was an independent predictor of DR according to multivariate regression analysis (OR=1.197, $p=0.009$). DR could be predicted with 92% sensitivity and 84% specificity when MHR was 16.05, whereas DR was predicted with 100% sensitivity and 98% specificity when MHR was 23 in ROC curve analysis (AUC: 0.356, 95% CI 0.251–0.460, $p = 0.008$). This study showed that patients with T2DM may be more likely to develop DR when they have high MHR values. Based on these results, clinicians can also use MHR as a new laboratory marker to predict DR.

The multivariate analysis revealed that WBCs count, monocytes, urea, creatinine, and MHR were significantly associated with diabetic nephropathy and proliferative diabetic retinopathy.

This result agrees with Tang *et al.* (2021) cross-sectional study, conducted at Sun Yat-sen University, Guangzhou, China. A total of 771 patients with T2DM and 607 healthy controls were enrolled in this study. MHR determination, ESR, CRP, ACR, blood urea, serum creatinine, and eye examination were performed. There was a significant association between monocytes, urea, creatinine, MHR, DN, and DR.

Concerning the sensitivity and specificity of MHR as a predictor of DN and DR among T2DM patients, our result shows that MHR is a highly sensitive predictor of microvascular complications in diabetic patients with Sensitivity (96%) and Specificity (73.3%).

5. Conclusion

MHR was significantly higher in diabetic patients with microvascular complications such as nephropathy and retinopathy. MHR could be used as an easy and cheap method for the prediction of early diabetic nephropathy and retinopathy. DN and DR have a positive correlation with MHR. MHR

is an independent predictor for the presence of DN and DR. MHR is highly sensitive to increased ACR.

References

Alrawahi, A. H., S.G.A.Rizvi, D. Al-Riami and Z.Al-Anqoodi, 2012. Prevalence and Risk Factors of Diabetic Nephropathy in Omani Type 2Diabetics in Al-Dakhiliyah Region. Oman Med. J. 27, 212.

Assmann, G. & A.M. Gotto, 2014. HDL Cholesterol and Protective Factors in Atherosclerosis. Circulation 109,

Çakır, Işıl, et al., 2020. "Monocyte to High-Density Lipoprotein Ratio: A Novel Inflammation Marker Related to Diabetic Retinopathy." Erciyes Medical Journal/Erciyes Tip Dergisi 42.2

Cho, N. H. et al., 2018. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes Res. Clin. Pract. 138, 271–281

Engerman, R. L., 2015. Pathogenesis of Diabetic Retinopathy. Diabetes 38, 1203–1206 .

Erdem, B. & Y. Kaya, 2021. Prediction of diabetic retinopathy in patients with type 2 diabetes mellitus by using monocyte to high-density lipoprotein-cholesterol ratio. Int. J. Diabetes Dev. Ctries. 1–6

Guariguata, L. et al., 2014. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res. Clin. Pract. 103, 137–149

Hirano, T., 2014. Abnormal lipoprotein metabolism in diabetic nephropathy. Clin. Exp. Nephrol. 18, 206–209

Karatas, Ahmet, et al., 2018. "Monocyte to high-density lipoprotein cholesterol ratio in patients with diabetes mellitus and diabetic nephropathy." Biomarkers in Medicine 12.9 953-959

Liu, J. et al., 2018. The association of neutrophil to lymphocyte ratio, mean platelet volume, and platelet distribution width with diabetic retinopathy and nephropathy: A meta-analysis. Biosci. Rep. 38,

Mikolasevic, I., M. Žutelija, V. Mavrinac, & L. Orlic, 2017. Dyslipidemia in patients with chronic kidney disease: etiology and management. Int. J. Nephrol. Renovasc. Dis. 10, 35

Naghavi, M. et al., 2015. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 385, 117–171.

Nentwich et al., 2015. Microvascular complication of diabetes mellitus . –abstract (2015) - 1016568.html.

Niveditha, H., C. Yogitha, P. Liji, S. Sundeep, N.V.V Himamshu, B.V. Vinutha & P. Pooja, 2013. Clinical correlation of HbA1c and diabetic nephropathy with diabetic retinopathy. Journal of Evolution of Medical and Dental Sciences, 2(49), 9430-9436.

Onalan, E., 2019. The relationship between monocyte to high-density lipoprotein cholesterol ratio and diabetic nephropathy. Pakistan J. Med. Sci., 35, 1081

Orban, J. C., E.Van Obberghen, & C. Ichai, 2017. Chronic Complications of Diabetes. Metab. Disord. Crit. Ill Patients From Pathophysiol. to Treat. 341–363

Pan, S. et al., 2017. Hamilton rating scale for depression-24 (HAM-D24) as a novel predictor for diabetic microvascular complications in type 2 diabetes mellitus patients. Psychiatry Res. 258, 177–183

Pathania, M., V. K. Rathaur, N.Yadav, A. Jayara and A.Chaturvedi, (2013). Quantitative Micro-albuminuria Assessment from 'Random Voided Urinary Albumin: Creatinine Ratio' Versus '24 hours Urinary Albumin Concentration' for Screening of Diabetic Nephropathy. J. Clin. Diagn. Res. 7, 2828

Romero-Aroca, P. et al., 2018. Glomerular filtration rate and/or ratio of urine albumin to creatinine as markers for diabetic retinopathy: A ten-year follow-up study. J. Diabetes Res. 2018.

Shi, C. & E.G. Pamer, 2011. Monocyte recruitment during infection and inflammation in diabetes mellitus. Nat. Rev. Immunol. 11, 762–774

Shikata, K. & H. Makino, 2013. Microinflammation in the pathogenesis of diabetic nephropathy. J. Diabetes Investig. 4, 142–149

Tang, X. et al., 2021. Association of the Monocyte–to–High-Density Lipoprotein Cholesterol Ratio With Diabetic Retinopathy. Front. Cardiovasc. Med. 8, 707008

Ulu, S. M. et al., 2013. Neutrophil-to-Lymphocyte Ratio as a Quick and Reliable Predictive Marker to Diagnose the Severity of Diabetic Retinopathy. 15, 942–947

Xu, T. et al., 2017. The relationship between neutrophil-to-lymphocyte ratio and diabetic peripheral neuropathy in Type 2 diabetes mellitus. Medicine (Baltimore). 96,

Yau, J.W.Y. et al., 2012. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. Diabetes Care 35, 556–564.

Zhang, Xin-Xin, et al., 2020. Prevalence of diabetic nephropathy among Type 2 Diabetes in chins. Ann. Glob. Heal. 81, 814–820