Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

Homocysteine as a Screening and Diagnostic Indicator for Assessing Diabetic Retinopathy Risk in Patients with Diabetes Mellitus

Prof. Dr. Raef Malak Botros [1], Ahmed Mohamed Bahaa Eldin [2], Hany Khairy Mansour [1],Nesma Hussien Ahmed [1], Mona Ebrahem Sayed EL-deep [1]

Department of Internal Medicine and Endocrinology, Faculty of Medicine, [1] Ain Shams University, [2] Assiut University

Corresponding author: *Mona Ebrahem Sayed EL-deep*
Email*: mona.eldepp@gmail.com*
Phone*: 010061130642*

ABSTRACT

Background: Diabetes mellitus is a group of metabolic conditions defined by persistent hyperglycemia caused by a lack of insulin action, secretion, or both. Diabetic retinopathy (DR) is a serious consequence of diabetes mellitus (DM), which remains the largest cause of vision loss in working-age people.

Aim of the Work: To examine plasma homocysteine as a screening and diagnostic indicator for measuring diabetic retinopathy (DR) risk in diabetes mellitus patients.

Patients and Methods: Over the course of eight months, from April 2022 to December 2022, an observational study involving ninety diabetic patients at the diabetes outpatient clinic at Ain Shams University Hospital examined plasma homocysteine as a screening and diagnostic indicator for determining the risk of diabetic retinopathy (DR) in patients with diabetes mellitus.

Results: Our study show that there was a high statistically significant difference between the studied groups regarding (age of the patient and duration of diabetes mellitus) also clinical data (HTN, SBP and DBP) also laboratory data (FBS, HBA1C, eGFR and albumin /creatinine ratio). The study also show that there was a high statistically significant difference between the studied groups regarding homocysteine level. In our study there was positive correlation found between homocysteine level and (age, duration of diabetes, HbA1C and FBG, eGFR and ACR).In addition, there was no statistically significant difference between the studied groups regarding (gender, smoking and BMI).

Conclusion: One of the main complications associated with diabetes mellitus (DM) is diabetic retinopathy (DR). A noteworthy correlation was seen between the amount of plasma homocysteine and diabetic retinopathy. When used as an indication of diabetic retinopathy, plasma homocysteine is a practical and reliable test for determining if diabetic individuals have DR.

Keywords: Homocysteine, Assessing Diabetic Retinopathy, Diabetes Mellitus

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders marked by persistently high blood sugar levels due to insufficient insulin production, action, or both. which cause several organs, namely the heart, blood vessels, kidneys, nerves, and eyes, to suffer long-term harm and impairment ***(ADA, 2021).***

Ninety-five percent of diabetes patients will eventually develop diabetic retinopathy (DR), one of the most serious microvascular consequences of diabetes mellitus (DM) ***(Bennett et al., 2017)***. Considering that 3–8% of those with type 1 diabetes are predicted to go blind ***(Broe et al., 2014)***. There are two primary categories of diabetic retinopathy: proliferative and nonproliferative. The term "proliferative" describes the presence or absence of neovascularization, or the development of aberrant blood vessels, in the retina. Regretfully, DR may continue undiagnosed or unnoticed until blindness and permanent damage have occurred ***(Kashim, 2018).***

An amino acid that contains sulfur, homocysteine (Hcy), is produced during the metabolism of methionine. By generating free radicals, high plasma homocysteine levels are harmful to the

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org
SJIF 2020: 6.224
IFS 2020 4.085

vascular endothelium. By rupturing the endothelium's integrity and revealing the smooth muscle and vascular matrix underneath, these free radicals directly harm the endothelium. This promotes a hypercoagulability state by activating platelets and thrombus formation ***(Elias and Eng, 2005)***. According to ***Lim et al. (2012)***, it causes oxidative stress and is involved in the oxidation-reduction process. Additionally, it has been linked to vascular disorders through pro-proliferative and endotoxic effects that may disrupt methylation processes and glutathione production ***(Chen et al., 2002).***

Given that diabetes is a microvascular occlusive disease, the fact that homocysteine levels are greater in proliferative diabetic retinopathy than in nonproliferative diabetic retinopathy may be explained by an adjuvant risk factor that raises plasma homocysteine levels and causes a hypercoagulability condition ***(Goldstein et al., 2004).***

The study found that the PDR patients had mean blood levels of Hcy that were higher than those of the NDR control group; however, this difference was not statistically significant ***(Gupta et al., 2018)***. According to ***Xu et al. (2014)***, a different research revealed that patients with DM who had PDR had greater plasma levels of Hcy than patients who had neither DR nor NDR. Research has demonstrated that individuals with PDR who had an increased Hcy in their vitreous following vitreoretinal surgery most likely had the blood-retina barrier breaking down ***(Gupta et al., 2018).*** Conversely, several investigations found no discernible difference in Hcy levels between individuals with proliferative retinopathy and those without it; nonetheless, patients with proliferative retinopathy have much greater homocysteine levels than those without it ***(Vaccaro et al., 2000).***

AIM OF THE WORK

The study objective is to look at plasma homocysteine as a screening and diagnostic marker for determining a patient's risk of developing diabetic retinopathy (DR) in individuals with diabetes mellitus.

SUBJECTS AND METHODS

Type of Study:

This research is an observational one. The study was carried out in the diabetes outpatient clinic at Ain Shams University Hospital between April 2022 and December 2022. Participants were chosen at random based on the inclusion and exclusion criteria of the study. Ninety patients total were used in this study, split into two groups: group A consisted of thirty diabetic patients without diabetic retinopathy, while group B consisted of sixty diabetic patients with the condition. Two subgroups were created from Group B: Group B1 consisted of thirty diabetic patients with nonproliferative DR, and Group B2 consisted of thirty diabetic patients with proliferative DR.

Inclusion criteria:

Diabetic patients having a diabetes mellitus history of at least 10 years, including type 1 and type 2, both sexes.

Exclusion criteria:

Patients with chronic liver disease, eGFR less than 60 mL/min/1.73 m2, and vascular or inflammatory conditions known to raise homocysteine levels, such as a recent stroke or myocardial infarction.

All patients were asked to provide a complete history, including their diabetes mellitus history (age of onset, duration, treatment doses, compliance of treatment). General examination: Vital data (pulse, blood pressure), anthropometric measures (weight, height, BMI (Weight/(Height in meters)^2))

Laboratory investigations

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

FBS, PPBS (mg/dl), HBA1C (%), Estimated GFR (mL/min/1.73m2), Serum plasma homocysteine (Umol/L) and Albumin/creatinine ratio (mg/g).

Fundus examination

An specialist ophthalmologist at Ain Shams University Hospital's Ophthalmology outpatient clinic performed a fundus examination and graded diabetic retinopathy. The ophthalmoscope was used after pupillary dilation with 1% tropicamide and 10% phenylephrine eye drops. Retinopathy was classified according to the findings in the worse eye. The fundus was examined using a binocular indirect ophthalmoscope (Keeler Instruments Inc. PA, USA) and a slit lamp biomicroscope (Magnon SL-450, Japan) equipped with a fundus lens.

Statistical analysis

Data were gathered, edited, tagged, and put into IBM SPSS version 23. The quantitative data with parametric distribution were given as mean, standard deviations, and ranges, whereas nonparametric data were presented as median with interquartile range (IQR). In addition, qualitative characteristics were reported as numbers and percentages. The p-value was deemed significant as follows: P-value > 0.05: non-significant (NS), P-value < 0.05: significant (S), and P-value < 0.01: highly significant (HS).

RESULTS

Table 1: Comparison between 3 groups as regards demographic data.

		Group A Normal fundus **(N=30)**	**Group B1** Non PDR **(N=30)**	**Group B2** PDR **(N=30)**	**P-value**
Age (years)		39.967 ± 12.121	44.767 ± 11.144	50.367 ± 7.247	0.001*
Gender	**Male**	8(26.67%)	9(30.00%)	12(40.00%)	#0.516
	Female	22(73.33%)	21(70.00%)	18(60.00%)	
Smoking	**No**	25(83.33%)	26(86.67%)	24(80.00%)	#0.787
	Yes	5(16.67%)	4(13.33%)	6(20.00%)	
BMI (kg/m²)		27.520 ± 5.123	28.680 ± 5.472	29.050 ± 4.633	0.481

*#Chi-Square test, • ANOVA test, *significant, N: number of patients.*

All three groups under study were matched for sex, and while there was no statistically significant difference in terms of smoking or BMI, there was a significant difference in terms of age.

Table 2: Comparison between 3 groups as regards clinical data.

		Group A Normal fundus **(N=30)**	**Group B1** Non PDR **(N=30)**	**Group B2** PDR **(N=30)**	**P-value**
Duration (years)		12.133±2.825	12.367±3.316	15.133±5.494	0.008*
HTN		5(16%)	13(43%)	17(56%)	0.001*
DM Treatment	**Oral antidiabetics**	3(10.00%)	4(13.33%)	6(20.00%)	#0.075
	Insulin	14(46.67%)	12(40.00%)	4(13.33%)	
	Both	13(43.33%)	14(46.67%)	20(66.67%)	

*#Chi-Square test, • ANOVA test, *significant, N: number of patients.*

There was a high statistically significant difference between the studied groups regarding duration of DM, hypertension.

Table 3: Comparison between 3 groups as regards laboratory investigations.

	Group A Normal fundus **(N=30)**	**Group B1** Non PDR **(N=30)**	**Group B2** PDR **(N=30)**	**P-value**

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

FBG(mg/dl)	165.967±69.689	225.033 ± 83.468	239.267±92.152	0.002*
2HPP(mg/dl)	239.333±108.599	254.867±81.332	259.867±81.386	0.663
HBA1C(%)	8.540±2.482	9.137 ± 2.314	10.443±3.391	0.029*
eGFR(mL/min/1.73m2)	98.367 ± 9.353	91.833 ± 6.701	81.233±6.484	<0.001*
ACR (mg/g)	24.333±7.203	40.700±18.925	213.833±55.209	<0.001*

• *ANOVA test, *significant.*

In terms of FBG, HbA1c, eGFR, and ACR, there was a significant statistical difference between the groups under study; however, in terms of 2-hour PPBG, there was no statistically significant difference between any of the groups under study.

Table 4: Comparison between three groups as regards Homocysteine level.

	Group A Normal fundus	**Group B1** Non PDR	**Group B2** PDR	**•P-value**	**A& B1**	**A &B2**	**B1& B2**
ɒmocysteine (Umol/L)	11.653 ± 3.745	19.473 ± 5.853	22.573 ± 9.353	<0.001*	**“** <0.001*	**“** <0.001*	**“** 0.181

• *ANOVA test, *significant, “TUKEY’S Test*

Between the groups under investigation, there was a substantial statistical difference in homocysteine levels (p-value 0.001). While there was no statistically significant difference between group B1 and group B2, there was a substantial statistically significant difference in homocysteine levels between group A and group B1 (p-value 0.001) and between group A and group B2 (p-value 0.001).

Table 5: Homocysteine level in subclasses according to hypertension state in studied patients.

Hypertensive state	**N**	**Mean ±SD**	**P-value**
No	55	14.969±5.485	^ <0.001*
Yes	35	22.506±9.390	

^ *independent T test, *significant, N=number of patients.*

A comparison of the homocysteine levels in hypertension and non-hypertensive individuals revealed a substantial statistical difference, with the homocysteine levels in hypertensive patients being greater (P value <0.001).

Table 6: Homocysteine level in subclasses according to diabetes treatment (oral antidiabetics, insulin orboth) in studied patients.

Diabetic treatments	**N**	**Mean ±SD**	**P-value**
Oral antidiabetics	13	24.454±12.148	^0.001*
Insulin	30	14.947±6.807	
Both	47	17.972±6.430	

^ *independent T test, *significant, N=number of patients.*

Also comparison of homocysteine level between patients on different treatment modalities showed a high statistically significant difference being higher with oral antidiabetics P value (0.001)**.**

Table 7: Correlation study of homocysteine level and other parameters

Correlations								
	Homocysteine							
	Group A Normal fundus **(N=30)**		**Group B1** Non PDR **(N=30)**		**Group B2** PDR **(N=30)**		**All patients(N=90)**	
	r	**P-value**	**r**	**P-value**	**r**	**P-value**	**r**	**P-value**
Age (Years)	0.320	0.085	0.087	0.647	-0.209	0.268	0.232	0.028*
Duration (Years)	0.150	0.428	0.153	0.418	0.404	0.027*	0.382	<0.001*
BMI (kg/m²)	0.227	0.228	-0.151	0.426	-0.106	0.577	0.033	0.755

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

HBA1C (%)	0.047	0.805	-0.168	0.376	0.436	0.016*	0.313	0.003*
FBG (mg/dl)	0.182	0.336	-0.196	0.299	0.427	0.019*	0.355	0.001*
2HPP (mg/dl)	0.000	0.998	-0.211	0.264	0.033	0.864	0.022	0.839
GFR (mL/min/1.73m2)	-0.127	0.502	-0.075	0.695	0.116	0.540	-0.364	<0.001*
ACR (mg/g)	0.025	0.894	-0.248	0.187	-0.169	0.373	0.360	<0.001*

**significant, N=number of patients.*

Upon conducting correlation study age, duration of diabetes, HbA1C and FBG, eGFR and ACR were positively correlated with homocysteine level. While there was no correlation between homocysteine level BMI and 2hpp**.**

Table 8: Multivariable binary logistic regression.

Linear regression	**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**P-value**
	B	**S.E**	**Beta**		
Age (years)	0.000	0.005	-0.004	-0.059	0.953
Duration (years)	-0.002	0.011	-0.010	-0.186	0.853
HBA1C (%)	-0.032	0.022	-0.112	-1.469	0.146
FBG (mg/dl)	0.001	0.001	0.146	1.882	0.063
Homocysteine (Umol/L)	0.024	0.006	0.241	3.848	<0.001*
GFR (mL/min/1.73m2)	-0.011	0.007	-0.144	-1.703	0.092
ACR (mg/g)	0.006	0.001	0.622	9.215	<0.001*
HTN	0.064	0.093	0.038	0.696	0.489
Dependent Variable: Fundus					

*S.E: standard error, t: indipendant t test, * significant.*

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

ACR and homocysteine level were shown to be risk factors for diabetic retinopathy when multivariable binary logistic regression was used to identify predictors of the condition.

DISCUSSION

Diabetes retinopathy (DR) is the most prevalent microangiopathic consequence of the disease. Increasing evidence suggests that systemic inflammation plays an important role in the development and progression of DR in both the early and late phases, stimulating the production of new blood vessels and macular edema, disrupting the glial cross, and causing neuronal loss ***(Lange et al., 2016).***

Homocysteine is harmful to the vascular endothelium because it produces free radicals. These free radicals induce direct harm to the endothelium by disturbing its integrity and exposing the underlying vascular matrix and smooth muscle, therefore encouraging hypercoagulability through platelet activation and thrombus formation ***(Elias and Eng, 2005).***

Inner and outer BRB integrity is disrupted by elevated homocysteine. Homocysteine damages the structural and functional integrity of the retina and raises BRB permeability. Retinal ischemia, neovascularization, vascular leakage, and a weak blood–retinal barrier are signs of altered retinal vasculature linked to homocysteine ***(Ibrahim et al., 2016).***

The purpose of our study was to examine the use of plasma homocysteine as a screening and diagnostic marker for determining the risk of diabetic retinopathy (DR) in individuals with diabetes mellitus.

According to our research, there was a substantial statistical difference (p value <0.001) in the age of the groups under investigation. This may be explained by the fact that as people age, arteriosclerotic alterations in the retinal arteries become noticeable. In the event of diabetes or hypertension, these alterations intensify even more. In turn, arteriosclerosis facilitates the development and progression of diabetic retinopathy.

This outcome is consistent with the findings of ***Lima et al. (2016) and Forga et al. (2016),*** who discovered that the incidence of diabetic retinopathy rose with patient age.

Lima et al. (2016) discovered, in contrary to our research, that a patient's age is not a risk factor for diabetic retinopathy. This discrepancy might be explained by variations in participant characteristics, race or ethnicity, and research methodology.

According to our research, there was a significant statistical difference (p-value of 0.008) in the length of DM between the groups under investigation. The impact of persistent hyperglycemia on retinal vessels may account for this. Systemic inflammation brought on by diabetes mellitus damages the glial cross and results in neuronal death. These factors are crucial in the onset and progression of diabetic retinopathy. They also induce the production of new blood vessels and macular edema.

This finding is consistent with the findings of ***Niazi et al. (2010) and Voigt et al. (2018),*** who discovered a high incidence of retinopathy and a strong correlation between it with the length of diabetes mellitus.

According to our research, diabetic individuals with PDR had a greater prevalence of hypertension. This can be explained by the fact that alterations in tiny arteries resulting from hypertension raise overall peripheral resistance to blood flow, which may hasten the development of diabetic retinopathy.

These findings are consistent with those of ***Liu et al. (2020),*** who discovered a strong correlation between poorly managed and untreated hypertension and diabetic retinopathy.

According to our research, there was a significant statistical difference between the groups under investigation in terms of the glycaemic profile (FBS and HbA1c), with diabetic individuals with PDR having higher values (P value: 0.002, 0.029), respectively. The phenomenon of

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

neovascularization can be attributed to the effects of chronic hyperglycemia, which include oxidative stress, thickening of the retinal capillary basement membrane, increased permeability of the retinal vascular system, tissue ischemia, and the release of numerous vasoactive chemicals.

This finding is consistent with studies by ***Forga et al. (2016), Yin et al. (2020), and Matsushita et al. (2020)*** that found a direct link between the onset and advancement of diabetic retinopathy and inadequate glycemic control as assessed by glycated hemoglobin and FBG.

According to our research, there was a substantial statistical difference between the groups under investigation in terms of eGFR and ACR, with the latter being greater in diabetic individuals with PDR (p value 0.001, 0.001), respectively. This could be explained by the pathogenesis of diabetic retinopathy and diabetic kidney disease (DKD) being similar. This includes oxidative stress caused by hyperglycemia, the buildup of advanced glycation end products, an increase in reactive oxygen species production, aberrant activation of protein kinase C, abnormal activation of the renin-angiotensin system, etc. This in particular could clarify the relationship between DR and DKD, which shows up in ACR as one DR-predictive factor.

This finding is consistent with the prospective observational studies conducted by ***Lee et al. (2015), Rossing et al. (2002), and Zhuang et al. (2019),*** which discovered a correlation between the stages of DR and eGFR and ACR.

According to our research, there was no gender-related statistically significant difference between the groups under investigation (p value 0.516). This could be explained by the fact that there was no sex selection and our trial was randomised.

This outcome concurs with the findings of ***Magliah et al. (2018) and Warwick et al. (2017),*** who also found no evidence of a significant correlation between gender and diabetic retinopathy.

Forga et al. (2016) discovered that males were more likely than women to develop diabetic retinopathy, which is contrary to the findings of our study. This discrepancy might be explained by variations in participant characteristics, race or ethnicity, and research methodology.

According to our research, there was no statistically significant difference in smoking between the groups under examination (p value 0.787). The relationship between the preponderance of females in our study and our Egyptian culture may help to explain this.

This finding is consistent with that of ***Magliah et al. (2018),*** who discovered that smoking does not increase the chance of developing diabetic retinopathy.

Contrary to what we discovered, smokers had a much higher chance of developing diabetic retinopathy ***(Cai et al., 2018).*** This discrepancy might be explained by variations in participant characteristics, race or ethnicity, and research methodology.

According to our research, there was no statistically significant variation in the patients' BMI between the groups under investigation (p value 0.481).

Zhou et al. (2017) and Magliah et al. (2018) reported that a high BMI is not a risk factor for diabetic retinopathy, which is consistent with our findings.

Conversely, research by ***Price et al. (2014) and De Block et al. (2005)*** showed that obesity was the main risk factor for retinopathy. This discrepancy might be explained by variations in participant characteristics, race or ethnicity, and research methodology.

According to our research, there was a significant statistical difference between the groups under investigation when it came to the homocysteine level, which was greater in PDR patients (p value <0.001). This can be explained by the fact that, as diabetes mellitus is a microvascular occlusive illness, elevated levels of plasma Hcy, an adjuvant risk factor that contributes to a state of hypercoagulability, may hasten the onset or progression of diabetic retinopathy. Because hcy is toxic to the vascular endothelium, it causes thrombosis and may aggravate hypoxic states like those associated with diabetic retinopathy.

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

This outcome is consistent with the findings of ***Brazionis et al. (2008), Lei et al. (2018), and Gupta et al. (2018),*** who discovered that diabetic patients with retinopathy had mean plasma total homocysteine concentrations that were greater than those of non-retinopathy. Additionally, they discovered that individuals with PDR had mean plasma total homocysteine concentrations that were greater than those of non-PDR patients.

According to our research, there was a statistically significant difference in homocysteine levels between individuals with hypertension and those without (p value<0.001). The correlation between homocysteine and hypertension can be explained by the fact that both conditions cause endothelial dysfunction and increased arterial stiffness, which in turn reduces nitric oxide availability.

This finding is consistent with the findings of ***Stehouwer and van Guldener (2003) and Skeete et al. (2017),*** who discovered that hypertension is a risk factor for elevated plasma homocysteine levels.

In our investigation, there was a highly statistically significant difference in homocysteine levels between treatment modalities, with individuals receiving oral antidiabetics having greater homocysteine levels (p value).

This outcome is consistent with a research by ***Looker et al. (2003),*** which discovered that the mean homocysteine concentration was greater in individuals on oral anti-diabetics than in those receiving insulin.

This study revealed a favorable relationship between the length of DM, FBG, and HA1C, and the homocysteine level.

This outcome is consistent with a research by ***Zulfania et al. (2018),*** which discovered a substantial positive connection between homocysteine and the length of diabetes mellitus.

This outcome is consistent with a research by ***Satyanarayana et al. (2011),*** which discovered that the homocysteine level increased with the levels of FBG and HbA1c.

According to our research, there was no statistically significant difference in homocysteine levels between males and females.

The findings of ***Zhao et al. (2021)*** who discovered that gender is not a risk factor for elevated plasma homocysteine (Hcy) levels are consistent with this outcome.

This finding contradicts that of ***Xu et al. (2020),*** who discovered that males had considerably greater Hcy levels than females. This discrepancy might be explained by variations in participant characteristics, race or ethnicity, and research methodology.

According to our research, there was no statistically significant difference in homocysteine levels between smokers and nonsmokers. This may be explained by the tiny percentage of smokers in our study, which is a result of the correlation between the study's female preponderance and our Egyptian culture.

This finding contradicts a ***2004*** research by ***Sobczak et al.*** that found smoking to be a risk factor for elevated plasma homocysteine (Hcy) levels. This discrepancy might be explained by variations in participant characteristics, race or ethnicity, and research methodology.

Our findings indicate that serum homocysteine levels rise dramatically and are extremely significantly related with FPG and HbA1c in diabetic patients when compared to HbA1c and FPG (diabetes metabolic management).

According to the current study, raised homocysteine, which is greater in PDR patients than NPDR patients and normal fundus patients, is a useful and practical indicator for predicting the occurrence of DR in diabetic patients.

CONCLUSION

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

Elevated amounts of plasma homocysteine directly harm the vascular endothelium and trigger thrombosis, which exacerbates hypoxic conditions such diabetic retinopathy.

Since plasma homocysteine is greater in PDR patients than NPDR patients and may be used as a diagnostic of diabetic retinopathy, it is a practical and useful metric for predicting the existence of DR in diabetic patients.

REFERENCES

American Diabetes Association (ADA). (2021) Diagnosis and classification of diabetes mellitus. Diabetescare: 40(1): S11-S24.

Bennett GH and Tuthill A (2017): Investigating the Barriers to the Uptake of Diabetic RetinaScreen. IrMed J. 110(9):628.

Brazionis L, Rowley K, Itsiopoulos C, et al. (2008): Homocysteine and diabetic retinopathy. Diabetes Care.
31(1):50-6.

Broe R, Rasmussen ML, Frydkjaer-Olsen U, et al. (2014): The 16-year incidence, progression and regression of diabetic retinopathy in a young population-based Danish cohort with type 1 diabetes mellitus: The Danish cohort of pediatric diabetes 1987 (DCPD1987). Acta Diabetol. 51(3):413-20.

Cai X, Chen Y, Yang W, et al. (2018): The association of smoking and risk of diabetic retinopathy in patients with type 1 and type 2 diabetes: a meta-analysis. Endocrine. 62(2):299-306.

Chen C, Conklin BS, Ren Z and et al. (2002): Homocysteine decreases endothelium-dependent vasorelaxation in porcine arteries. J Surg Res. 102(1):22-30.

De Block CE, De Leeuw IH and Van Gaal LF (2005): Impact of overweight on chronic microvascular complications in type 1 diabetic patients. Diabetes Care. 28(7):1649-55.

Elias AN and Eng S (2005): Homocysteine concentrations in patients with diabetes mellitus--relationship to microvascular and macrovascular disease. Diabetes Obes Metab. 7(2):117-21.

Forga L, Goñi MJ, Ibáñez B, et al. (2016): Influence of Age at Diagnosis and Time-Dependent Risk Factors on the Development of Diabetic Retinopathy in Patients with Type 1 Diabetes. J DiabetesRes. 2016:9898309.

Goldstein M, Leibovitch I, Yeffimov I, et al. (2004): Hyperhomocysteinemia in patients with diabetes mellitus with and without diabetic retinopathy. Eye (Lond). 18(5):460-5.

Gupta P, John D, Rebekah G, et al. (2018): Role of hyperhomocysteinemia in proliferative diabetic retinopathy: A case-control study. Indian J Ophthalmol. 66(10):1435-1440.

Ibrahim AS, Mander S, Hussein KA, et al. (2016): Hyperhomocysteinemia disrupts retinal pigment epithelial structure and function with features of age-related macular degeneration. Oncotarget. 7(8):8532-45.

Kashim RM, Newton P and Ojo O (2018): Diabetic Retinopathy Screening: A Systematic Review on Patients' Non-Attendance. Int J Environ Res Public Health. 15(1):157.

Lange C, Storkebaum E, De Almodóvar CR, et al. (2016). Vascular endothelial growth factor: a neurovascular target in neurological diseases. Nature Reviews Neurology; 12(8):439-54.

Lee R, Wong TY and Sabanayagam C. (2015): Epidemiology of diabetic retinopathy, diabetic macular edema and related vision loss. Eye Vis (Lond). 2:17.

Lei X, Zeng G, Zhang Y, et al. (2018): Association between homocysteine level and the risk of diabetic retinopathy: a systematic review and meta-analysis. Diabetol Metab Syndr. 10:61.

Lim CP, Loo AV, Khaw KW, et al. (2012): Plasma, aqueous and vitreous homocysteine levels in proliferative diabetic retinopathy. Br J Ophthalmol. 96(5):704-7.

Lima VC, Cavalieri G C, Lima M C, et al. (2016): Risk factors for diabetic retinopathy: a case–control study. International journal of retina and vitreous, 2(1), 1-7.

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

Liu L, Quang ND, Banu R, et al. (2020): Hypertension, blood pressure control and diabetic retinopathy in alarge population-based study. PLoS ONE 15(3): e0229665.

Looker HC, Fagot-Campagna A, Gunter EW, et al. (2003): Homocysteine as a risk factor for nephropathyand retinopathy in Type 2 diabetes. Diabetologia 46, 766–772.

Magliah SF, Bardisi W, Al Attah M, et al. (2018): The prevalence and risk factors of diabetic retinopathy in selected primary care centers during the 3-year screening intervals. J Family Med Prim Care. 7(5):975-981.

Matsushita Y, Takeda N, Nakamura Y, et al. (2020): A Comparison of the Association of Fasting Plasma Glucose and HbA1c Levels with Diabetic Retinopathy in Japanese Men. J Diabetes Res. 2020:3214676.

Niazi MK, Akram A, Naz MA, et al. (2010): Duration of diabetes as a significant factor for retinopathy. Pakistan Journal of Ophthalmology, 26(4).

Price SA, Gorelik A, Fourlanos S, et al. (2014): Obesity is associated with retinopathy and macrovascular disease in type 1 diabetes. Obes Res Clin Pract. 8(2):e178-82.

Journal of research in health science
Volume 8 issue. 1-2 2024, pp. 57-68
ISSN 2523-1251 (Online) ISSN 2523-1243 (Print)
JOURNAL DOI 10.37057/2523-1251
www.journalofresearch.org
info@journalofresearch.org

SJIF 2020: 6.224
IFS 2020 4.085

Rossing P, Hougaard P and Parving HH. (2002): Risk factors for development of incipient and overt diabetic nephropathy in type 1 diabetic patients: a 10-year prospective observational study. Diabetes Care. 25(5):859-64.

Satyanarayana A, Balakrishna N, Pitla S, et al. (2011): Status of B-vitamins and homocysteine in diabetic retinopathy: association with vitamin-B12 deficiency and hyperhomocysteinemia. PLoS One. 6(11):e26747.

Skeete J and DiPette DJ. (2017): Relationship between homocysteine and hypertension: New data add to the debate. J Clin Hypertens (Greenwich). 19(11):1171-1172.

Sobczak A, Wardas W, Zielinska-Danch W, et al. (2004): The influence of smoking on plasma homocysteine and cysteine levels in passive and active smokers. Clin Chem Lab Med. 42(4):408-14.

Stehouwer CD and van Guldener C. (2003): Does homocysteine cause hypertension? Clin Chem Lab Med. 41(11):1408-11.

Vaccaro O, Perna AF, Mancini FP, et al. (2000): Plasma homocysteine and microvascular complications in type 1 diabetes. Nutr Metab Cardiovasc Dis. 10(6):297-304.

Voigt M, Schmidt S, Lehmann T, et al. (2018): Prevalence and Progression Rate of Diabetic Retinopathy in Type 2 Diabetes Patients in Correlation with the Duration of Diabetes. Exp Clin Endocrinol Diabetes. 126(9):570-576.

Wong TY, Cheung N, Tay WT, et al. (2008): Prevalence and risk factors for diabetic retinopathy: the Singapore Malay Eye Study. Ophthalmology. Nov;115(11):1869-75.

Xu C, Wu Y, Liu G, et al. (2014): Relationship between homocysteine level and diabetic retinopathy: a systematic review and meta-analysis. Diagn Pathol. 9:167.

Xu R, Huang F, WangY, et al. (2020): Gender- and age-related differences in homocysteine concentration:a cross-sectional study of the general population of China. Sci Rep 10, 17401.

Yin L, Zhang D, Ren Q, et al. (2020): Prevalence and risk factors of diabetic retinopathy in diabetic patients: A community based cross-sectional study. Medicine (Baltimore). 99(9):e19236.

Zhao, J., Li, Z., Hou, C. et al. (2021): Gender differences in risk factors for high plasma homocysteine levels based on a retrospective checkup cohort using a generalized estimating equation analysis. Lipids Health Dis 20, 31.

Zhou Y, Zhang Y, Shi K, et al. (2017): Body mass index and risk of diabetic retinopathy: A meta-analysis and systematic review. Medicine (Baltimore). 2017; 96(22):e6754.

Zhuang X, Cao D, Yang D, et al. (2019): Association of diabetic retinopathy and diabetic macular oedema with renal function in southern Chinese patients with type 2 diabetes mellitus: a single-centre observational studyBMJ Open 9:e031194.

Zulfania L, Khan A, Rehman S, et al. (2018): Association of homocysteine with body mass index, blood pressure, HbA1c and duration of diabetes in type 2 diabetics. Pak J Med Sci. 34(6):1483-1487.