Unravelling the Influence of Demographic and Lifestyle Factors on Monocyte Chemoattractant Protein-1 in Diabetic Retinopathy Patients

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ABSTRACT

Objectives: To determine the association of Monocyte chemoattractant protein-1 (MCP-1) level with Age, blood glucose level, Exercise, Gender and Smoking in diabetic retinopathy patients.

Study Design and settings: A case-control study was carried in the physiology department at the Jinnah Postgraduate Medical Centre in Karachi From April 2019 to October 2020.

Methodology: One hundred people were divided into four groups which were; Group D (n=25) were healthy normal individuals; Group C (n=25) diabetic patient's with moderate retinopathy; Group B (n=25) diabetic patient's with mild retinopathy while Group A (n=25) diabetic patients with no retinopathy. Every participant was checked for blood sugar level, retinoscopy through slit lamp examination and serum MCP-1 level. The association was made between diabetic retinopathy, MCP-1 protein levels, age, gender, smoking and exercise.

Results: MCP-1 levels are significantly greater in diabetic males with moderate retinopathy compared to diabetic females with moderate retinopathy (p-value 0.042). Similarly, smoking is associated with the elevation of MCP-1 levels in diabetic patients with moderate retinopathy (p-value 0.05). Exercise has no significant effect on MCP-1 levels in all groups. An increase in age, HbA1C, fasting and random blood glucose levels were significantly correlated with MCP-1 levels (p-value 0.000)

Conclusion: It is concluded from the study that an advance in age and an increase in blood glucose level are associated with an increased level of MCP-1 protein. Moreover, Male gender and smoking are also associated with enhanced MCP-1 levels in diabetic patients with moderate retinopathy.

Keywords: Diabetic Retinopathy, Exercise, Gender, Monocyte Chemoattractant Protein-1, Smoking.

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INTRODUCTION:

Diabetes mellitus, also known as simply diabetes, is a metabolic disorder that causes an increased level of glucose in the blood.[1] Diabetes mellitus could be caused by a dysfunction in insulin secretion (type I), a dysfunction in insulin action on receptors (type II), gestational diabetes, or secondarily by using drugs like steroids.[2] Diabetic retinopathy, also known simply as DR, is a common complication of diabetes that can result in permanent vision loss. Within the age range of 20 to 74 years old, it is one of the leading causes of blindness. There are 15.9 percent of people in the population who have diabetic retinopathy (DR).[3] Macular edema degeneration and the development of new blood vessels, which can lead to glaucoma, are both caused by hyperglycemia. Hyperglycemia also contributes to the pathology that occurs in the retinal microvasculature. There are two different varieties of diabetic retinopathy: proliferative retinopathy and non-proliferative retinopathy. The most common form of diabetic retinopathy is known as non-proliferative diabetic retinopathy, and one trait that distinguishes it from proliferative diabetic retinopathy is the absence of new blood vessel growth. A condition known as

proliferative diabetic retinopathy occurs when certain blood vessels in the eye become blocked due to persistently high blood sugar levels. At the same time, new blood vessels begin to emerge; if the blood vessels become blocked, fibrosis and retinal detachment may develop in the area where they are blocked.[4] A further complication of diabetic retinopathy is known as diabetic macular edema. In this condition, the macula swells and becomes thicker, which reduces one's field of vision.[5] The length of time a person has diabetes plays a significant role in how far along they are in their diabetic condition. The symptoms of DR include a blurred or distorted field of vision, a reduction in visual acuity, black spots, and visual impairment. All of these things happen due to microvascular destruction of the retina, atherosclerotic changes of the retinal vein, retinal haemorrhage, and retinal detachment.[6] Diabetic retinopathy starts to progress after five years in patients with type I diabetes, while in type II diabetes, many patients already have retinal modification at the time of diagnosis.[7] An annual examination of the retina is something that is advised for all diabetic patients. It is possible to postpone the onset of diabetic retinopathy as well as the progression of the condition by exercising stringent control over one's blood sugar levels.[8] Cytokines, which are also known as chemokines, are categorized according to their capacity to attract particular types of chemokine. MCP-1 is a type of chemokine that regulates the infiltration and migration of immune cells such as monocytes and macrophages. It plays an essential role in the maturation of immune and inflammatory responses.[9] It is believed that MCP-1 is an important indicator of diabetic retinopathy and that it could be used as a diagnostic marker of diabetes. MCP-1 is a pro-inflammatory cytokine that causes damage to the retina by inducing inflammation caused by the migration of leukocytes to the retina.[10] Different cells of the retina will overexpress themselves for MCP-1 if the diabetic condition is not under control. When this happens, a cascade of reactions will occur in the retina, and as a result, the retina's vascularity will increase, eventually leading to diabetic retinopathy (DR).[11]

Diabetic retinopathy must be detected in its earliest stages if one is to avoid irreversible vision loss and achieve better overall patient outcomes. Diabetic retinopathy can be managed more effectively and with less risk to the patient's vision if it is detected at a non-progressive stage when it first appears. In addition, diabetic retinopathy can be detected and treated early, which can result in lower overall healthcare costs and fewer complications over the long term. MCP-1 is a recently discovered marker that has the potential to be utilized in the process of determining the prognosis for diabetic retinopathy patients. Only a few studies have attempted to stratify risk variables for MCP-1 levels in diabetic retinopathy patients. The objective of this study is to investigate the influence of factors such as age, blood glucose levels, gender, smoking, and physical activity on the amount of monocyte chemoattractant protein 1 in diabetic individuals who have retinopathy.

METHODOLOGY

After the approval from the Ethical review board, this case-control study was conducted at the department of Physiology, Basic Medical Science Institute, Karachi from April 2019 to October 2020. In this study, 100 participants between forty to sixty-five years of age were selected from the Ophthalmology department JPMC Karachi. Open EPI was used to calculate the sample size. Anticipating the frequency of diabetic retinopathy as 6.7% and considering the population at the maximum value of 1 million, the estimated sample size came to 97. Diabetic patients were included on the basis of criteria of the American Diabetic association 18. After a detailed history, Patients were examined by a consultant ophthalmologist through slit lamp examination and fundoscopy. The patients were divided into four groups; Group A (n=25) comprised diabetic patients without retinopathy; Group B (n=25) comprised diabetic patients with mild retinopathy features; Group C (n=25) comprised diabetic patients with moderate retinopathy features while Group D (n=25) were normal healthy individuals. Patients with vitreous, macular detachment, cataract, severe diabetic retinopathy, myocardial disease stroke, renal or hepatic insufficiency and bleeding disorder were excluded from the study.

After taking informed written consent, overnight fasting blood samples of the patients were taken. Serum was taken from blood and then stored at -80ºc, and then blood sugar and MCP-1 levels were estimated with the help of the ELISA method. The basic demographic features of the study participants were calculated and presented in terms of frequencies. An Independent sample t-test was applied to determine the difference in MCP-1 levels in the male and female gender, smokers and non-smokers and exercise and lack of exercise group. Diabetic patients who were doing brisk walk for 30 minutes or performing any form of exercise were included in exercise group. or Pearson's correlation was used to determine the correlation of age, blood glucose level and HBA1C levels with MCP-1 level. Data were analyzed by using SPSS version 22.0.

RESULTS:

The study participants' mean age was 53.17 + 6.36 years. A total of 100 participants were included in the study. Among them 40 were female and 60 were male. In each group, 15 were male, and 10 were female participants. Basic demographic features of the study participants is shown in Table 1. It has been found that levels of MCP-1 in males and females of groups A (diabetics with no retinopathy) and group B (diabetics with mild retinopathy) are proportionally equal to each other. In group C (diabetics with moderate retinopathy) level of MCP-1 in male patients is significantly greater than in female patients, whose p-

value is 0.042, which is significant. It has been found that level of MCP-1 in smokers and in non-smokers of group A and B are comparably equal to each other. In group-C among smokers, the MCP-1 level is more significant when compared to non-smokers patients (p-value 0.05). No significant difference in MCP 1 level was found when we compared all four groups in association with exercise, as shown in Table 2. An increase in age, HbA1c, fasting and random blood glucose levels were significantly correlated with MCP-1 levels (p-value 0.000), as shown in Table 3.

DISCUSSION:

Diabetes mellitus is a very common metabolic disease that can transform into a metabolic syndrome involving different organs like kidneys, cardiovascular system, nervous system and eyes. Among these, diabetic retinopathy is a common consequence of DM that can progress toward visual loss and blindness. The likelihood of DR increases with duration and poor glycemic control of the disease. Patients of DM type I are more prone to develop DR as compared to those of DM type II[12]. This study has discussed the relationship between MCP-1 and diabetic retinopathy as a diagnostic indicator.

It has been found that there is an increased level of serum MCP-1 in patients of DR in all the three groups having

diabetes and diabetic retinopathy due to overexpression of MCP-1 acting as inflammatory chemokine causing retinal impairment in DR. It is also evident from our results that in those patients who have a longer duration of DR have a greater value of serum MCP-1. In another study conducted by Reddy et al and Taghave et al it was found that MCP-1 serum level increases with the progression of severity and duration of DM and DR[13]. In another study by Urbancic et

Table 1: Basic demographic features of study participants

Variable	N %
Sex	
Male	60 (60%)
Female	40 (40%)
Living Area	
Rural	40 (40%)
Urban	60 (60%)
Maritial status	
Married	93 (93%)
Unmarried	7 (7%)
Socioeconomic status	
Poor	17 (17%)
Middle	71 (71%)
Upper	12 (12%)
Education	
Illiterate	11 (11%)
Till higher secondary school certificate	64 (64%)
Bachelor's or higher education	25 (25%)
Smoking status	
Smoker	43 (43%)
Non-smoker	57 (57%)
BMI	
Ideal	34 (34%)
Overweight	59 (59%)
Obese	7 (7%)

Table 2: Impact of gender, smoking and exercise on MCP-1 level in study participants distributed according to diabetic retinopathy stages.

Variable	Mean + SD	Mean + SD	P-value
Gender	**Male** N=60	**Female** N=40	
Diabetes without retinopathy	(n=15) 127.54+16.74	(n = 10) 122.72+10.01	.423
Diabetes with Mild retinopathy	(n=15) 344.09+21.56	(n = 10) 342.64+17.32	.860
Diabetes with Moderate retinopathy	(n=15) 517.44+50.8	(n = 10) 481.6+15.7	.042*
Healthy subjects	(n=15) 18.72+3.54	(n = 10) 18.28+6.30	.852
Smoking Status	**Smoker (N=43)**	**Non-smoker (N=57)**	
Diabetes without retinopathy	(n=12) 127.22+18.08	(n=13) 124.13+10.45	.602
Diabetes with Mild retinopathy	(n=12) 344.28	(n=13) 342.67	.843
Diabetes with Moderate retinopathy	(n=11) 522.13+39.5	(n=14) 488.14+42.47	.05*
Healthy subjects	(n=8) 18.16+2.23	(n=17) 18.72+5.57	.788
Exercise status	**Exercise**	**No exercise**	
Diabetes without retinopathy	(n=12) 121.65+11.95	(n=13) 129.27+15.89	.191
Diabetes with Mild retinopathy	(n=16) 345.95+21.92	(n=9) 339.16+14.78	.418
Diabetes with Moderate retinopathy	(n=19) 501.84+44.59	(n=6) 507.08+45.30	.805
Healthy subjects	(n=7) 17.77+4.40	(n=18) 18.84+4.92	.620

Table 3: Correlation of MCP-1 levels with Age, FBG, RBG & HBA1C

Variable	r-value	p-value
HbA1c	.865	.000
RBG	.920	.000
FBG	.899	.000
Age	.694	.000

al. and Behfar et al., they found increased MCP-1 as an early indicator of the onset of inflammation and progression of DR, which can be used as a tool to identify DR in its early phase of disease[14,15]. Mitra et al have suggested that DR is more common in uncontrolled hyperglycemic patients, which promotes cellular injury in retina.[16]

In our study, we have further divided these groups based on gender and then found that the male population has a greater value of serum MCP-1 than females, especially in those with a longer duration of diabetic retinopathy as in group C of our study. Another study conducted by James et al on MCP-1 comparison with parameters like gender and age found that the level of MCP-1 is found to be greater in the male population, which is consistent with our study[17].

In our other parameter, we have found that smokers have a greater value of MCP-1 in all the groups compared to non-smokers. A study conducted by Komiyama et al found a positive correlation between smokers and MCP-1 protein and in our study, we have also found results similar to the above study.[18] Another study conducted by feng et al found that there is an increased level of chemokines like MCP-1 and CRP compared to that of non-smokers which also supports our study[19].

In this study, exercise shows no significant difference in MCP-1 serum levels between different study groups. In another study conducted by Marloes et al found that there is no effect of exercise on serum MCP-1 and leptins levels in female population[20]. Marius et al conducted a study on the effect of exercise on the serum level of MCP-1 and interleukin in which they found that there is no increase in serum MCP-1 level in metabolic conditions like atherosclerosis and Diabetes[21].

Patients with diabetic retinopathy with uncontrolled diabetes and advanced age should be checked regularly. However, more studies should be conducted to ascertain the association of gender and smoking with increased MCP 1 levels in diabetic retinopathy patients.

CONCLUSION:

It is concluded from the study that there is an increased level of MCP-1 protein found in moderate diabetic retinopathy patients, especially among males and the smoker population. Exercise couldn't affect the level of MCP-1 protein. An advance in age and an increase in blood glucose level are associated with an increased level of MCP-1 protein.

Authors Contribution:
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Hammad Raziq: Final Drafting
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Sana Soomro: Concept design Data Collection
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