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ASSOCIATION BETWEEN INSULIN RESISTANCE AND MCP-1 LEVEL IN TYPE 2 DIABETIC FOOT ULCER OF IRAQI PATIENTS

Mariam Riyadh Obied*[1], Fadhil Jawad Al-Tu'ma[2], Amir Kareem Sultan[3] and Hameed Hussein Al-Jameel[4]

[1,2]Department of Biochemistry, College of Medicine, University of Kerbala / Kerbala – Iraq.
[3]Department of Surgery, General Surgeon, Al-Hussein Teaching Hospital, Al-Hussein Medical City, Kerbala Health Directorate / Kerbala – Iraq.
[3]Department of Internal Medicine, College of Medicine, University of Kerbala / Kerbala – Iraq.

***Corresponding Author: Mariam Riyadh Obied**

Department of Biochemistry, College of Medicine, University of Kerbala / Kerbala – Iraq.

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ABSTRACT

Background: The one of Diabetes Mellitus (DM) complication is Diabetic foot ulcer (DFU), it is retard wound healing and the limbs may end with amputation. For the prevention of DFU, it has been necessary to take preventive measures that lead to reduce the amount of amputation to more than 50 %. The adipocytes secreted Monocyte chemoattractant protein-1 (MCP-1) is a member of the CC chemokine family and plays a vital role in the inflammatory process. has been linked with DFU and parameters of insulin resistance**. Objective:** To evaluated the correlation between serum MCP-1 concentration and other clinical characteristics in Iraqi DFU subjects. **Materials and Methods:** A cross-sectional study was done on 235 subjects, including 135 with DFU and 100 with Type 2 Diabetes Mellitus (T2DM) without DFU. Phenotypic data, comprising serum MCP-1 level, lipid profile, blood glucose, insulin, C-peptide and HOMA-IR were investigated. **Results:** This study included from 61% male and 38% female. While, the distribution of DFU group according to the age groups the higher incidence is in (55-64 years) age group. There was non-significant difference in age and gender between DFU and non-DFU group (P-value >0.05 for both). The serum MCP-1 concentration was significantly correlated with HOMA-IR and insulin among DFU group, while, HbA1c and TG was positively correlated with MCP-1 level in non-DFU group. **Conclusion:** 1. We found non-significant difference in age and gender between DFU and non-DFU group 2. A significant positive correlation was found between MCP-1 serum level, fasting insulin and HOMA-IR among T2DM with DFU group.

KEYWORDS: DFU, T2DM, MCP-1, HOMA-IR.

INTRODUCTION

Diabetes Mellitus (DM) is a group of chronic, metabolic diseases characterized by high levels of blood glucose resulting from defects in insulin action, production or both and metabolic abnormalities in carbohydrates, proteins, and fats.[1,2] Worldwide, with 425 million people diagnosed with DM in 2017, the number is expected to reach to 629 million by 2045 according to the report of the World Health Organization.[3,5]

The complications of diabetes are DFUs and are intended for people with diabetes with a variety of specialties, circulatory system, and acute neurological disorders and musculoskeletal. The risk of foot infection in diabetics is high. In diabetics, these foot ulcers are constantly infected and have potential for cellulite development, and if not treated promptly and appropriately, they lead to inflammation of the blood, gangrene, and amputation.[6] However, for the prevention of DFU, it has been necessary to take preventive measures, which involve identifying individuals with risk factors for foot ulcers, educating the patient and colleagues in the field of foot care and appropriate and comprehensive treatment of foot ulcers, the amount of amputation can be reduce to more than 50 %.[7]

Insulin resistance is a characteristic feature of T2DM associated with obesity or metabolic syndrome. the secreted of Adipocytokines, including leptin, retinol-binding protein 4 (RBP4), adiponectin, and MCP-1, by adipocytes which are seem to be implicated with pathogenesis of insulin resistance linked with obesity.[8]

The secreted of a chemokine Monocyte chemoattractant protein–1 (MCP–1) by many cells including retinal pigment epithelial cells and lymphocytes. It regulates monocyte chemotaxis and endothelial activation and modulates the inflammatory processes.[9] the positive correlations between the serum MCP-1 level and

HOMA-IR that have been reported by many recent studies in human.[8]

The aim of this study was to find the relationship between the levels of MCP-1 with insulin resistance and other parameters in Iraqi DFU patients.

MATERIALS AND METHODS

In this cross-sectional study, the total number of 135 subjects with DFU and 100 subjects with T2DM with non-DFU were randomly chosen. The study was carried out during the period of Nov 2018 to July 2019 in the Al-Hassan Center for Endocrinology at the Al-Hussein Medical City/Kerbala Health Directorates/Kerbala, Iraq.

Blood sample (5 ml) was taken from each group, the serum utilized for various biochemical investigations, including (lipid profile, HbA1c, Insulin, C-peptide, blood glucose and MCP-1 level). The MCP-1 protein level was measured by ELISA, the insulin and C-peptide were automatic calculation by using the ARCHITECT PLUS i 1000 SR, and the other biomarkers were assessed, using the Roche COBAS c311.

Averaged data are presented as the means ± SD. Pearson's correlation test was done in order to test any correlation among the values of the above parameters in patients with DFU. A P value of < 0.05 was considered statistically significant.

RESULTS

The current study included 235 subjects (135 patients with DFU and 100 with T2DM without DFU). According to gender the distribution of the DFU group were 61% male and 38% female was shown in fig 1. while, the distribution of non-DFU group were 56% male and 44% female.

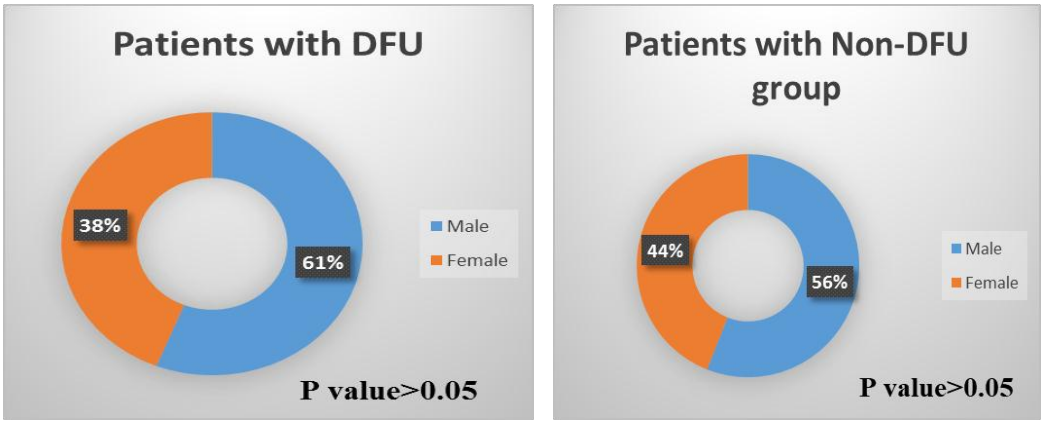

Figure 1: Gender distribution of the study individuals.

However, patient's distribution according to age groups were 3% (35-44 years), 25% (45-54 years), 41% (55-64 years) and 28% (65-74 years) was shown in fig 2. the higher incidence of DFU is in (55-64 years) age group. There was non-significant difference in age and gender between DFU and non-DFU group (P- value >0.05 for both).

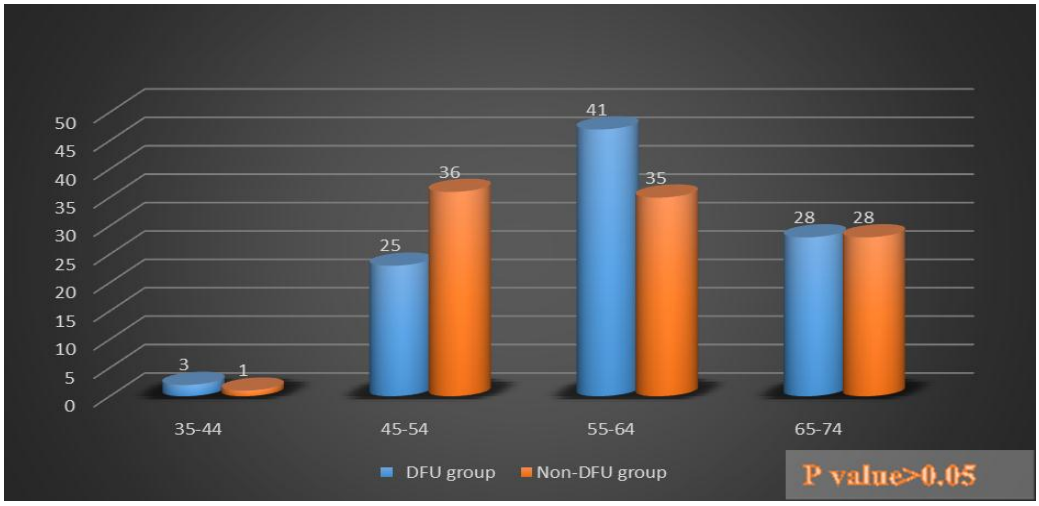

Fig. 2: Subjects distribution according to age groups.

In the present study, the relationship between (Insulin, C-peptide, MCP-1, HOMA-IR, TG, TC, and LDL-C) was significant with DFU group (P-value <0.05 However, there was non-significant difference between (VLDL-C and HDL-C) with DFU group table 1.

Table 1: Biochemical characteristics of DFU and non-DFU patients.

Parameter	DFU group Mean ±SD	Non-DFU group Mean ±SD	P value
Insulin(µu/ml)	21.01±8.601	13.61±6.60	**0.001***
C-peptide(ng/mL)	2.64±0.99	2.17±0.993	**0.001***
MCP-1 level(pg/ml)	236.2±99.94	193.2±85.28	**0.001***
HOMA-IR	13.69±6.6	9.23±3.9	**0.001***
TC(mg/dl)	196.98± 37.93	162.4±37.15	**0.001***
TG(mg/dl)	205.14±96.95	173.1±55.6	**0.005***
LDL-C(mg/dl)	136.74± 32.53	106.8±39.4	**0.001***
HDL-C(mg/dl)	39.39±10.64	37.07±7.5	0.09
VLDL-C(mg/dl)	37.72±10.25	35.75±12.52	0.1
Blood glucose(mg/dl)	247.8±88.67	195.9±80.2	**0.001***
HbA1c%	10.17±1.99	10.26± 2.5	0.79

Student t test was used, *significant P< 0.05.

A significant positive correlation was found between MCP-1 serum level with Insulin, HOMA-IR among DFU group. While, HbA1c and TG was positively correlated with MCP-1 level in non-DFU group table 2.

Table 2: Correlation between serum MCP-1 concentration and other clinical characteristics in DFU and non-DFU patient.

Clinical characteristics	MCP-1 level(pg/ml)			
	DFU group		Non-DFU group	
	Correlation	P-value	Correlation	P-value
C-peptide(ng/mL)	-0.04	0.89	-0.070	0.485
Insulin(uU/mL)	**0.65****	**0.04***	-0.183	0.0682
HMOA-IR	**0.51****	0.12	-0.153	0.127
Blood sugar(mg/dl)	-0.11	0.75	-0.032	0.748
HbA1c%	-0.02	0.94	**0.059****	0.556
TG(mg/dl)	-0.12	0.73	**0.025****	0.80
TC(mg/dl)	-0.25	0.47	-0.222	**0.029***
HDL-C(mg/dl)	-0.11	0.75	-0.283	**0.004***
LDL-C(mg/dl)	-0.21	0.55	-0.180	0.072
VLDL-C(mg/dl)	-0.12	0.73	-0.000	0.996

***Significant P < 0.05, **positive correlation.**

DISCUSSION

In many studies the greater incidence of diabetic women was more than men, which can be attributed to their gender characteristics, but then in terms of complications, men developed DFU more than women.[10]

The predominate male patients were developing DFU, which was consistent with other studies.[11] and.[12] This could be explained by the fact that men have more outside activity than have women, which may lead to more foot exposure to different risks and more plantar pressure on their feet.[13]

In the study of Xiaolei Li included 71 men and 50 women.[14] while the study of frykberg et al., 90.3% of the population were male.[15] and in the study of Tan and colleagues, the number of men and women was equal.[16]

There is no significant difference in age between DFU and non-DFU group. This age matching helps to eliminate differences in parameters' results that may originate due to the significant variation in age.

Analysis results shown that the T2DM and DFU group were age–sex matched (P-value >0.05 for both). This is identical to a study of Xiaolei Li.[14]

The relationship between (insulin and blood glucose level) and DFU group was significantly different, this means that people who had more blood sugar, had more severe leg ulcers. This agrees with study of Rasisfar et al.[6]

The relationship between blood glucose and DFU prevalence was a signficant. While, In the study of Dekker, there was a significant relationship between

HbA1c and the incidence of diabetic foot disorders.[17] The recent study results showed that improved blood glucose control can improve wound healing.[18] The most of cells in the body needs insulin to allow glucose to enter the blood and the medium between the cells and into the cells; if eating a diet rich in sugar and large starches, the pancreas is unable to produce enough insulin to enter sugar into cells or able to secrete sufficient insulin in the bloodstream, but the cells unable to use glucose due to insulin resistance, thus remains part of sugar in the blood; T2DM results in the non-conversion of glucose into energy, resulting in excessive amounts of blood glucose.[7]

In the present study, the relationship between triglyceride, cholesterol and LDL was significant with DFU group (P-value <0.05) table 1. However, there was non-significant difference between VLDL and HDL with DFU group (P-value > 0.05). These results agree with those of.[19-21]

Type 2 diabetes is characterized by hyperglycemia and dyslipidemia which associated with a cluster of risk factors forming the metabolic syndrome and leads to serious complications. High levels of glucose (and cholesterol) leads to macro and micro vascular diseases. The high hyperglycemia (carbohydrate metabolic disorder) in diabetic patients leads to neuropathy. How the nerves are injured is not entirely clear but research suggests that high blood glucose changes the metabolism of nerve cells and causes reduced blood flow to the nerve. Neuropathy and vascularopathy alone or together can cause diabetic foot ulcerations.[22]

There were non-significant differences in HbA1c between DFU and non-DFU groups table 1. As in the study of Xiaolei Li.[14]

Uncontrolled HbA1c level is considered to be a strong indicator of uncontrolled glucose level in blood. The study of Hasan, et al.[20] evaluated the level of HbA1c levels in diabetic patients having DFU and without DFU, while, the relationship among MCP-1 level and DFU group were significant. This is identical to the study of Van Asten and colleagues suggested that the MCP-1 expression level was increased in patients with DFU.[23] The serum concentration of MCP-1 was strongly correlated with DFU.[24] the production of MCP-1 in vascular endothelial cells and its abnormal expression can enhance by hyperglycemia, that may contribute to the complications related to angiogenesis and vascular functions among T2DM patients.[25]

In T2DM, the patients with high levels of MCP-1 were more likely to develop diabetic complications.[26,27] Furthermore, the upregulation of MCP-1 in patients with DM may lead to abnormal leukocyte infiltration in ulcerative tissue.[24]

CONCLUSION

Accordingly, we can conclude that:

1. We found a non-significant difference in age and gender between DFU and non-DFU group.
2. A significant positive correlation was found between MCP-1 serum level, fasting insulin and HOMA-IR among T2DM with DFU group.

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