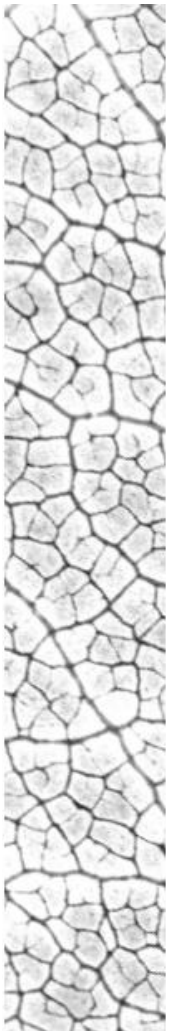

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Biochemical and haematological characteristics in patients with a type 2 diabetes mellitus in Baghdad, Iraq

May Jaleel Abed [1*], Ajile Al-Zamily [1], Ahmed Ghdhban Al-Ziaydi [1], Huda Kadhem Mohsen [1]

[1] Department of Medical Chemistry, College of Medicine, University of Al-Qadisiyah, IRAQ
*Corresponding author: may.abed@qu.edu.iq

Abstract
The objective of this study was to compare the hematological and biochemical profiles of patients with or without diabetes mellitus type 2 (DM2), to report the differences in the Iraqi population and the factors associated with diabetes in a population under a hemodialysis (HD) management. A retrospective observational study, where the clinical analyses of three patients with DM2 and three patients without DM2 who visited the University Hospital, Baghdad were reviewed between December 2017 and December 2018 for treatment of (HD) Patients with DM2 were defined by the previous diagnosis. The present work has some limitations. The studies are from a single-center, they are made in Baghdad, which does not allow extrapolating the results to other regions of the country. Results identified that Diabetes is a significant issue related to inflammation, anemia, lymphopenia, and monocytosis in patients undergoing HD. In this series of patients, MRL was the most powerful marker of inflammation. This evidence needs to be corroborated by larger studies.

Keywords: diabetes mellitus, kidney disease., diabetic nephropathy, haemodialysi

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INTRODUCTION

Chronic kidney disease (CKD) is a public health issue due to its development, complications and complex comorbidity like diabetes mellitus (DM) (ADA, 1997). DM is a chronic disease in Iraq with a prevalence of 7.4% according to our latest study (Ali *et al*, 2019). In Iraq, DM is a disease that affects thousands of people and is the fifteenth cause of death in the country (Almahfoodh *et al,* 2017). Diabetic nephropathy (DN) is the main artery problem, the world's leading cause of CKD and it motivates dialysis admission (Atlas, 2015). The pathogenesis of DN is not fully understood and the induction of inflammation by hyperglycemia may be the main cause (Schena & Gesualdo, 2005). In the last century, the prevalence of DN was 40.5% among patients with CKD. Currently, this prevalence has increased to 50% and patients with DN are part of the 60% annual deaths of patients on hemodialysis (HD) (Mosher, 2011).

Mansour *et al* (2014) have been studied that the mortality analysis of a population prevalent in HD in a private center in Basrah, Iraq. The results were indicated that the main cause of CKD among its patients could be primary glomerulonephritis (CNG) with 32%, followed by DM with 22%. However, four years later in 2019, (Ali et al, 2019) were reported that by using mortality of the population incident in HD in Duhok, Erbil and Suleimania provinces in North of Iraq They concluded that the main cause of CKD among patients is DM with 44%, followed by the CNG with 23%. CKD which might also occur in patients without DMand they is identified as "non-diabetic renal disease" (NDRD) (Mami *et al*, 2017).

DN is difficult to reverse. However, certain NDRDs can be treatable. In this way, the therapy of DN and NDRDare different. A differential diagnosis of these two modalities is of considerable importance (Liang et al, 2013). Patients with CKD in HD have a defined pattern of their hematological profile with severe chronic anemia, normal or high white blood cell count and normal or low lymphocyte count. However, patients with CKD in diabetic HD have in addition to severe chronic anemia, lymphopenia and monocytosis (Wong *et al*, 2002). In the general population, obesity is one of the causes of DM and is associated with the high incidence of CKD in which inflammation is a common denominator of these metabolic abnormalities (Ejerblad *et al*, 2006). This research aimed to compare the hematological and biochemical parameters of patients with or without DM2, to report the differences in the Iraqi population selected

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from Baghdad Teaching Hospital, Baghdad, Iraq and the factors associated with diabetes in a population under an HD regime.

MATERIALS AND METHODS

The retrospective observational study was started from the first of December 2017 to the thirty-first of December 2018. All data were collected from 6 patients receiving therapy in the form of HD at the Baghdad Teaching Hospital, Baghdad, Iraq. In an attempt to add literature on the haematological and biochemical profile of diabetic patients in CKD and their relation to the amount of serum biochemical molecules. In addition to haematological parameters, Three diabetic patients were compared with three non-diabetic patients who had under an HD regimen.

These patients were administered 3 weekly sessions of conventional haemodialysis, with dose, adapted to guidelines embedded in the Global Guidelines on Therapy (ADA, 2010) to maintain KT / V valuesapplying the same kinetic model (2^{nd} generation) equal or greater than 1.2, changing, depending on this, the time of the haemodialysis session of the patients (from 210 to 240 minutes). The mean values and standard deviation (SD) of each haematological and biochemical parameter were obtained for 1 year (12 measurements in each patient). The complete blood cell count included haemoglobin, haematocrit, leukocytes, monocytes, eosinophil, basophils, lymphocytes and platelets. Within the inflammatory markers, platelets / lymphocyte ratio (PLR) was calculated by dividing the number of platelets between the number of lymphocytes and the neutrophil/lymphocyte ratio (NLR) by splitting the amount of neutrophils by lymphocyte count (Simmons *et al*, 2012). In turn, the MRL was calculated by dividing the number of lymphocytes by the number of monocytes. Quarterly values of total proteins (PT), plasma albumin (Alb) and total cholesterol (CT) were collected; and monthly transferrin (Tr), given its shorter half-life. The biochemical parameters also included TGP and TGO transaminases, triglycerides, alkaline phosphatase, low density Lipoprotein (LDL), high density Lipoprotein (HDL), C-reactive protein (PCR), calcium and serum phosphorus. The urea reduction percentage (PRU) was calculated by subtracting the initial urea concentration from the final urea concentration and dividing it by the initial urea percentage.

Ethical Considerations: The completion of the study required the approval of the Ethics Committee of the Medical Ethics, College of Medicine, and University of Baghdad. To carry out this work, all participants verbally accepted the informed consent where they received explanations authorizing the work by delivering their own results.

Statistical analysis : The comparison between groups, diabetic and non-diabetic, was performed using Student't' test. This analysis was performed using the MedCalc software (USA) statistical program. A probability (*p* value) <0.05 was considered statistically significant.

RESULTS

This study was started from first of December 2017 to thirty-first of December 2018. All data were collected from 6 patients receiving therapy in the form of HD at the Baghdad Teaching Hospital, Baghdad, Iraq. In an attempt to add literature on the haematological and biochemical profile of diabetic patients in CKD and their relation to the amount of serum biochemical molecules in addition to haematological parameters, we compared 3 diabetic patients (mean age 51.3 ± 11.59) with 3 non-diabetic patients (mean age 51.3 ± 18.04) who are under an HD regimen.

We obtained our reults by using retrospective observational study. All data were collected from 6 patients receiving therapy in the form of HD. In an attempt to add literature on the haematological and biochemical profile of diabetic patients in CKD and their relation to the amount of serum biochemical molecules in addition to haematological parameters. The mean age around 51.3 ± 11.59 with 3 non-diabetic patients, and for the patients under an HD regimen the mean reach to 51.3 ± 18.04 who are under an HD regimen.

Table 1 shows the valuesresulting from the comparison of the laboratory tests of the haematological parameters studied. The average haematocrit in diabetic patients was 28.5 ± 1.44% compared to 34.3 ± 1.55% in non-diabetic patients ($p<0.05$). Marked to moderate anaemia was found in both groups: 8.9 ± 0.12 g / dl in diabetic patients and 10.8 ± 0.75 g / dl in non-diabetic patients ($p<0.05$). The normal leukocyte mean was generally within normal values, ranging from 4 to 10.5 x 109 / l, with a mean of 7762 ± 445.30 x mm^3 in diabetic patients and 7987 ± 2104.10 x mm^3 in non-patients diabetics (not significant); however, there is a surprising monocytosis (13.9 ± 1.82%) in diabetic patients when compared to non-diabetics (9.00 ± 0.57%) ($p<0.05$). The mean lymphocyte percentage was lower in diabetic patients 19.3 ± 1.01 and 26.1 ± 0.31% in non-diabetic patients ($p<0.05$), although the neutrophil count in diabetic patients (60.8 ± 3.08) was not significant with the neutrophil count in non-diabetic patients (59.3 ± 1.95).

The platelet count was between 186 and 391 x 10^3 / mm^3 (mean 263 ± 111.61 x 10^3 / mm^3 in patients with diabetes and 224 ± 56.66 x 10^3 / mm^3 in non-diabetic patients (non-significant difference). NLR and PLR are considered low-cost markers as indicators of inflammation characteristic of DN (Khandare *et al*, 2017). In this study, NLR and PLR were introduced as

Table 1. Haematological parameters. Average blood count results of patients undergoing hemodialysis

	DM2			MEDIAN ±SD	NO DM2			MEDIAN ±SD	NORMAL	p-Value	p<0.05
HEMATOLOGICAL ANALYSIS	PATIENT 1	PATIENT 2	PATIENT 3		PATIENT 1	PATIENT 2	PATIENT 3				
Leukocytes	7642	7389	8255	7762±445.30	5895	10103	7964	7987±2104.10	5-10000 mm^3	0.86471	
Neutrophils	60	64.2	58.2	60.8±3.08	60.2	57.1	60.7	59.3±1.95	46-74 und	0.55524	
Eosinophil's	7.4	3.9	5.4	5.6±1.76	4.5	6.5	4.8	5.3±1.08	1-4 und	0.81335	
Basophils	0.7	0.3	0.9	0.6±0.31	0.2	0.5	0.4	0.4±0.15	0.2-1 und	0.24769	
Monocytes	12.3	13.6	15.9	13.9±1.82	9.2	9.5	8.4	9.0±0.57	02-8 und	11296	*
Haematocrit	26.9	29.6	29.1	28.5±1.44	32.7	34.3	35.8	34.3±1.55	33-46 %	0.00932	*
Haemoglobin	9	8.8	9	8.9±0.12	10.1	10.8	11.6	10.8±0.75	11-16 mg/dl	0.01064	*
Lymphocytes	19.9	18.1	19.8	19.3±0.01	26	26.4	25.8	26.1±0.31	20-40 und	0.00018	*
Platelets	391	212	186	263±111.61	188	289	194	224±56.66	150-450	0.61517	
NLR	3	3.6	2.9	3.2±0.38	2.3	2.2	2.4	2.3±0.10	<2	0.01856	*
PLR	19.7	11.7	9.4	13.6±5.41	7.2	11	7.5	8.6±2.11	>15	0.20753	
MRL	1.6	1.3	1.3	1.4±0.17	2.8	2.8	3	2.9±0.12	>4	0.0003	**

Data are expressed as mean ± ED. NLR: Neutrophil / lymphocyte ratio, PLR: platelets / lymphocyte ratio, MRL: lymphocyte / monocyte ratio
** extremely significant

Table 2. Biochemical parameters. Patient results in average

	DM2			MEDIAN ±SD	NO DM2			MEDIAN ±SD	V. NORMAL	p -VALUE
LIPID PROFILE	PATIENT 1	PATIENT 2	PATIENT 3		PATIENT 1	PATIENT 2	PATIENT 3			
Triglycerides	136.1	55.3	241	144.1±93.1	163	328	241	244±82.5	40-150 mg/dl	0.23684
Cholesterol	150.3	134.3	146	143.5±8.3	143.3	192.5	146	160.6±27.7	100-200 mg/dl	0.36379
HDL Cholesterol	47.7	38.7	23	36.5±12.5	31	28.5	23	27.5±4.1	>45 mg/dl	0.30312
LDL Cholesterol	93.3	86	73	84.1±10.3	85.8	92.3	73	83.7±9.8	60-180 mg/dl	0.96347
Pre- Urea	155.4	155.6	204	171.7±28	136.8	163.5	146.8	149.0±13.5		0.27576
Post- Urea	51.7	49.9	54.5	52.0±2.3	38.1	52.3	31.3	40.6±10.7	22-55 mg/dl	0.14427
Post Creatinine	6	4.2	5	5.1±0.9	4	6.2	3.5	4.6±1.4		0.63652
Hepatic Profile										
TGP	13.1	22.8	36	24.0±11.5	13.2	18.2	9.3	13.6±4.5	5-32 U/L	0.21783
TGO	15.2	21.5	20	18.9±3.3	10.2	11.8	6.5	9.5±2.7	7-33 U/L	0.01887
Alkaline Phosphates	117.2	364.3	78	186.5±155.2	232.7	85.3	157.5	158.5±73.7	30-120 U/L	0.79176
Total Proteins	7.2	7.6	7.9	7.6±0.4	7.2	7.3	7	7.2±0.2	6.4-8.3 g/dl	0.1447
Albumin	4.1	4.1	4.4	4.2±0.2	3.8	4.6	4.3	4.2±0.4	3.5-5 g/dl	0.90187
Reagent Protein C	1.8	4.3	0.4	2.2 ± 1.1	1.7	1.7	0.9	1.4 ± 0.03	<1 mg/L	0.56525
Electrolytes										
Serum Calcium	9	9.3	9.4	9.2±0.2	8.6	9.3	9.1	9.0±0.4	8.5-10.5 mg/dl	0.38665
Phosphorus	6.3	5.8	7.9	6.7±1.1	4.4	9.2	5.1	6.02±2.6	2.9-5 mg/dl	0.80297
Iron	5.4	8.5	10	8.0±2.4	10.7	10.7	8.6	10.0±1.2	10.7 -30.4uM/L	0.25319
Transferrin	207.2	181.8	164	184.3 ± 41	177	182.8	151.5	170.4 ± 29	200-400 mg/dl	0.4286
Ferritin	196	1563.7	1222	993.9±711.8	458.4	1318.6	305.7	694.2±546.1	28-365 mg/dl	0.59391
parathyroid hormone	191.7	32	234	152.6±106.5	742.4	116.3	347.3	402.0±316.6	50-300 pg/L	0.26555
PRU	0.67	0.68	0.73	0.69±0.03	0.72	0.68	0.79	0.73±0.1	>0.65	0.37916

Data are expressed as mean ± SD. PRU: Percentage reduction of urea. TGO and TGP: Transaminases

potential markers to determine inflammation in diabetic and non-diabetic patients doing HD. The mean NLR was significantly high in diabetic patients when compared to non-diabetic patients (mean NLR was 3.2 ± 0.38 in diabetic patients and 2.3 ± 0.10 in non-diabetic patients (p<0.05), although the mean of the PLRwas 13.6 ± 5.41 in diabetic patients and 8.6 ± 2.11 in non-diabetic patients respectively (not significant).

The most important finding of this study was monocytosis in that chosen population with DM and CKD when compared to patients without DM and CKD. Thus, a third marker of inflammation was highly significant among diabetic patients (MRL 1.4 ± 0.17) when compared to non-diabetic patients (MRL 2.9 ± 0.12) respectively. (p <0.0005). The processes of chronic inflammation associated with the dialysis technique are becoming increasingly relevant. **Table 2** shows that no statistically significant differences have been observed in the biochemical parameters evaluated, such as total proteins, albumin, total cholesterol and transferrin. Diabetic patients had higher CRP (2.2 ± 1.1 vs. 1.4 ± 0.03) and had similar total protein (PT) values (7.6 ± 0.1 vs. 7.3 ± 0, 01 g / dl) and transferrin (184.3 ± 41 vs. 170.4 ± 29 mg / dl). Proteinuria and serum calcium concentration did not demonstrate a significant relationship. ND is associated with variations in the value of liver profile molecules. In our research we only found significant differences in TGO transaminase (18.9) in diabetic patients vs. 9.5 in non-diabetic patients) (p <0.05). The values shown in **Tables 1** and **2** represent the average of the values taken during a year of follow-up and the results indicate that the hematological parameters have greater significance than the biochemical parameters in the comparison of diabetic and non-diabetic patients in HD.

DISCUSSION

Given that the two main risk factors for CKD, such as DM and arterial hypertension, are pathologies of increasing prevalence in Iraq interdisciplinary administrators as proposed by the Enhancing Global Outcomes Reinforced program should be included in this comprehensive strategy (Aldukhayel, 2017). Blood cells are a heterogeneous group of cells that can be

differentiated according to their phenotype and functional activity. Patients with CKD have many immune deficiencies secondary to the uremic state, including lymphopenia (Akbar, 2002). In this study, we found the low level of lymphocytes in diabetic patients demonstrating a greater degree of inflammation. The high number of platelets also reflects inflammatory conditions that include systemic infections, however, in the present study we found no significant differences in the number of platelets between diabetics and non-diabetics. Monocytes express surface molecules that combined with the antigen activate the inflammatory response (Shi & Pamer 2011).

The increase in this group of cells is associated with the chronic inflammation that characterizes patients in HD, however, in this study, the increase was more pronounced in diabetic patients when compared to non-diabetic patients. There are several biomarkers to determine inflammation in DN and its complications, such as the level of cytokines (Alqahtani *et al,* 2013). Systemic levels of inflammatory cytokines are elevated in patients with CKD and play a major role in the muscle catabolism of patients with CKD. However, clinical practice in our countries has difficulty obtaining these markers due to their high cost. Although the study shows that high PLR values are indicative of mortality (Hu *et al*, 2010), our work shows this trend in diabetic patients but is not significant when compared to the PLR of non-diabetic patients. Another study (Turkmen *et al*, 2012) also shows that patients with ECR and NLR ≥ 3.5 have significantly high levels of tumor necrosis factor-alpha (TNF-α) when compared to patients with NLR <3.5. In our study, this correlation was also significant when we compared diabetic and non-diabetic patients (3.2 ± 0.38 vs 2.3 ± 0.10).

Although MRL in peripheral blood could act as a prognostic marker in several solid tumors (Wang *et al,* 2017), in this study its prognostic value indicates a potent inflammatory marker in DN associated with HD. Our significant result in the NLR and MRL as new markers of inflammation in DN and its complications allows us to obtain them after a routine hematological profile. These data are new regarding the relationship between inflammation and DM in HD patients. Regarding significant anaemia in diabetic patients when compared to non-diabetic patients, it could be indicative of anaemia associated with CKD with more severe inflammatory processes. However, it should be noted that the majority of patients who perform hemodialysis have anemia due to the decrease in the production of erythropoietin due to the renal dysfunction itself. Participants with DM2 have a high prevalence of kidney function abnormalities relative to those (Mathur *et al,* 2016) without DM2. In our research, when compared to standard-diabetic patients, there is a substantial difference in the value of TGO creatine kinase in the 2-fold greater range in diabetic patients.

CONCLUSION

In conclusion, CKD is a frequent pathology with marked inflammatory problems more noticeable in patients with DN. Since inflammatory markers are connected to the development and/or progression of obesity, DM, and hypertension, the simple calculation of MRL, NLR, monocyte count, and lymphocyte count can predict increased inflammation in diabetic patients with RCT. Finding alternatives for the diagnosis, prevention, and treatment of DN is imperative. These data are part of a preliminary study; currently, we are dedicated to studying the pathophysiology of DN by analyzing the immunological parameters of patients suffering from CKD in HD. We believe that significant lymphopenia in diabetic patients may be due to lymphocyte trafficking and “homing” to other sites than the absolute number deficiency. The present work has some limitations. In the first place, the studies are from a single center which is located in Baghdad, which does not allow extrapolating the results to other regions of the country.

Despite this, it is an important study of this type on CKD and diabetes in Iraq and allows us to have a comprehensive view on important points to evaluate in future research with a better methodological design.

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