Study of Immunological Parameters, Hematologic Outcomes And Epidemiology Features of Renal Dysfunction Frequently in Karbala Province, Iraq

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Abstract

Renal failure or dysfunction: A disease occurs by a severe weakness in one kidney or both, they lose ability to do their functions effectively, resulting in the body's inability to remove waste and fluids, Leading to a significant changes in chemistry of blood and body fluid.

The study occurred in Karbala province where study samples were collected, which included (124). Samples divided in (64) patients and (60) control, patients had another division according to sex (44) male and (20) female. Immunologic parameters include (kidney injury molecules (KIM-1), pro-inflammatory TNF-α, IgG antibodies) Elabscience Kit, concentration in serum was massacred by (ELISA) Technique and hematologic test measured automatically by (Humlate plus-1 Device).

The results showed increase in kidney injury in age groups beyond the age of 40 years. A significantly higher incidence of disease among males more than females. Results show significant statically variations in serum levels:

1- kidney injury molecules (KIM-1) levels was increased in serum in patients significantly compare with control.

2- (TNF-α) levels was increased in patients than control.

3- IgG levels decreased in patients than control.

Another routine tests occurs to patients to know the effects of disease on blood variations, the test was included CBC count the results show CBC tests: (WBC, MHC, MCHC, RDWS, RDWC, PLT, PCT, PDWS, PDWC, P-LCC and P-LCR) have no significant differentials while CBC tests: (LYM., MON., GRA., RBC., HGB., HCT., MCV, MPV) which decrease in patient compare with control significantly.

Increase kidney injury and inflammatory in serum patients with disease, by measured some parameters levels in sera as indicators for disease progression and decrease in some antibodies such as IgG concentration of in sera, as well as the hematologic tests referrer to disease may associated with anemia.

Keywords: *Renal failure, (KIM-1), TNF-α cytokines. IgG antibodies, CBC test.*

Introduction

Kidney failure is a syndrome occurs when the kidney loses its ability to filter blood from toxins, along with several other factors that interfere with kidney dysfunction such as exposure to toxic substances, environmental contaminants, chemical preservatives and many renal failure diseases. Kidney failure (Renal disease) sometimes lead to death by accumulation of toxins in the body [(1)]. Etiology of renal insufficiency include loss of blood flow to the kidneys, resulting in heart failure, heart attacks, heart disease and liver cirrhosis, as well as dehydration, severe burns and infections, as well as the use of certain anti-inflammatory drugs. Some diseases and conditions lead to kidney failure such as exposure to blood clots, urinary hemolytic syndrome,

plasma cell carcinoma of the bone marrow, scleroderma, use of chemotherapy drugs, Priority [2]. Kidney failure is due to insufficient blood delivery to the kidneys for a long time result decrease in kidneys size, kidneys begin to shrink and slowly work until stopping or caused by a sudden blockage that affects the flow of urine from the kidneys [3] Acute kidney injury is common disease [4]. According to The National Institute for Health and Care Excellence refer that the epidemiology of renal failure is seen in approximately 13–18% in the world specially in elderly population [5]. Symptoms of renal failure are swelling of the legs, ankles and feet, undue distress in breathing, drowsiness or fatigue, nausea, confusion, pain or chest compression and other coma sometimes [6]. Kidney failure is diagnosed by urine analysis, by measuring the amount of urine, along with blood samples to measure the material that is filtered by the kidneys such as urea and creatinine [7]. Kidney injury molecule 1 is a protein . Its precise function is unknown, but elevated serum and urinary KIM-1 levels are associated with human renal injury, KIM-1 levels increased associated with histopathological evidence of kidney damage, fibrosis, and inflammation [8]. along with some imaging tests such as ultrasound, magnetic resonance imaging, And radiographic tomography [9]. Treatment of renal failure is through what is known as dialysis as an alternative to what the kidneys do in normal conditions, and the other treatment lies in kidney transplantation [10]. There are strong relationship between of kidney failure development and other risk factors can be minimized by age, sex, exposure for chemical toxicants, such as gases, tobacco, pesticides and other toxic products. Attention should be paid to the doctor's recommendations, appropriate treatment under his supervision and proper diet [11].

Current study pointed out on kidney failure disease, which is one of the most common diseases at present, by Establishing Demographic study to the patient of renal failure to show frequently diseases in patients according to aging, gender. Determent of renal failure by measured kidney injury molecule-1 as an indicator by ELISA technique. Estimate serum immunologic parameters such as TNF-α, IgG. Tacking the routine tests (CBC tests) for all patients with renal failure.

Materials and Method

1- Patients: Study type was identified as a study of patients' cases with renal failure compared to control. The samples were collected from the renal dialysis unit at Al Hussein Educational Hospital in Karbala city during the period of time 1/12/2018-15/3/2019. groups included 64 patients composed of (44) males and (20) females and healthy control (60) was apparent with no disease symptoms, based on clinical diagnosis by the physician and their health history. Data collected for patients including age and gender, some cases was excluded such as patients with hepatitis, Because of the and the interaction between patients and the impact of this on immune standards.

2- Blood sampling collection

5 ml of venous blood was collected in gel tubes for immunological studies; The serum was separated by Centrifuge (3,000 cycles for 5 minutes). The serum was then collected in sterile clean plastic tubes and kept in the refrigerator at -10 ° C until use. The serum was used to investigate the level.

Statically analysis: by ANOVA appropriate, X^2 test, students' independent T test, And *p* value (<0.05).

Results and Discussion

Demographic distribution of renal failure patients:

In current study which dealing with demographic, immunologic and hematologic parameters in Renal Failure patients in Karbala city. Distribution of Renal Failure patients according to study variables including (age, gender of renal failure) table (1). The number of current study (124) samples distribution according to age categories ranging from (>39-<51) year including (64) patients and 60 (control) and divided according to Gender (44) male and (20) female. The result show no significant in demographic data *P*. value more (<0.05). The *P*. value result recorded 0.33, according to the age and 0.15 according to the gender. According to the Age frequency disease is similar in categories (>39-<51) year respectively, while highly frequency (40-50) year. The results show the frequency of disease is increase in male more than female.

Table 1: Demographic distribution of renal failure patients (according to Age and Gender). (N=124)

Study Variable		percent patients	sample		Total	x2	*p*. value
			control				
Age	**>39**	Count	20	24	44	2.24	0.33
		% within age	45.5%	54.5%	100.0%		
		% of Total	16.1%	19.4%	45.2%		
	40-50	Count	24	24	56		
		% within age	50.0%	50.4%	100.0%		
		% of Total	19.4%	19.4%	38.7%		
	<51	Count	20	12	32		
		% within age	62.5%	37.5%	100.0%		
		% of Total	16.1%	9.7%	25.8%		
Gender	**male**	Count	44	48	92	2.05	0.15
		% within gender	47.8%	52.2%	100.0%		
		% of Total	35.5%	38.7%	74.2%		
	female	Count	20	12	32		
		% within gender	62.5%	37.5%	100.0%		
		% of Total	16.1%	9.7%	25.8%		

The data of the study showed about the demographic distribution that age groups after 40 years is the most vulnerable to the disease and the kidney failure as the results of the study is widespread in males compared with female. That refer to important demographic data (Age, Gender) effects on disease development. Kidney exposure during ageing to changes can be divided two parts namely: structural and functional [(12)]. Structural changes include: decreased kidney weight and volume; cortical atrophy, loss of renal parenchyma atrophy [(13)]. Kidney loss of functional glomeruli include decreased glomerular filtration rate, decreased effective renal plasma flow, increased impaired water, electrolyte, and glucose handling and decreased vasodilator activity of prostacyclin mechanisms for ageing-associated with increase oxidative stress [(14)]. Alterations in sexual responses and hormones can effected on kidney functions the cause may result from high levels of uremic toxins. [(15)]. Change in sex hormone such as decreases in testosterone levels and increases in prolactin levels, are common and cause erectile difficulties and decreased spermatocyte counts in male that can effect on kidney function [(16)].

Immunologic study of renal failure patients:

Immunologic parameters in current study as showed

in table (2) significant differences at (<0.05). The concentration of (KIM-1) molecules increase in serum of patients with Renal Failure (10.44±3.44 ng/ml) compare with control (0.78±1.25 ng/ml) at p. value (0.00) (Figure 1). Levels of pro-inflammatory TNF-α significantly higher in patients serum compared to control group where means have (151.81±81.69, 84.90±69.36 pg/ml) respectively (Figure 2). IgG registered decline (0.45±0.29 ng/ml) in patients than control (6.29±4.71 ng/ml) in sera (Figure 3).

Table 2: Immunologic parameters distribution between renal failure patients and control.

Study variable	Patients renal failure (Mean ± SD)	Control renal failure (Mean ± SD)	T test	P. values
Kidney injury molecule-1 (KIM-1) ng/ml	9.44±3.44	0.87±1.25	18.18	0.00
TNF-α Cytokines pg/ml	243.81±81.69	84.90±69.36	11.64	0.00
IgG Antibody ng/ml	0.50±0.29	7.29±4.71	-11.52	0.00

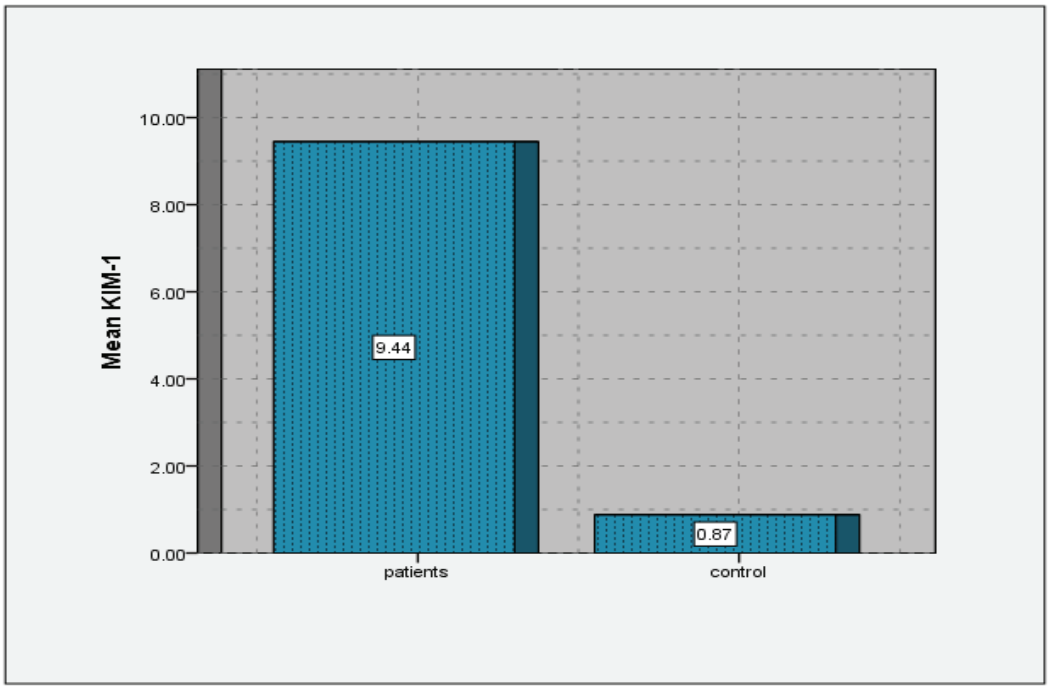

Figure 1: KIM-1 molecule levels in renal failure patients and control.

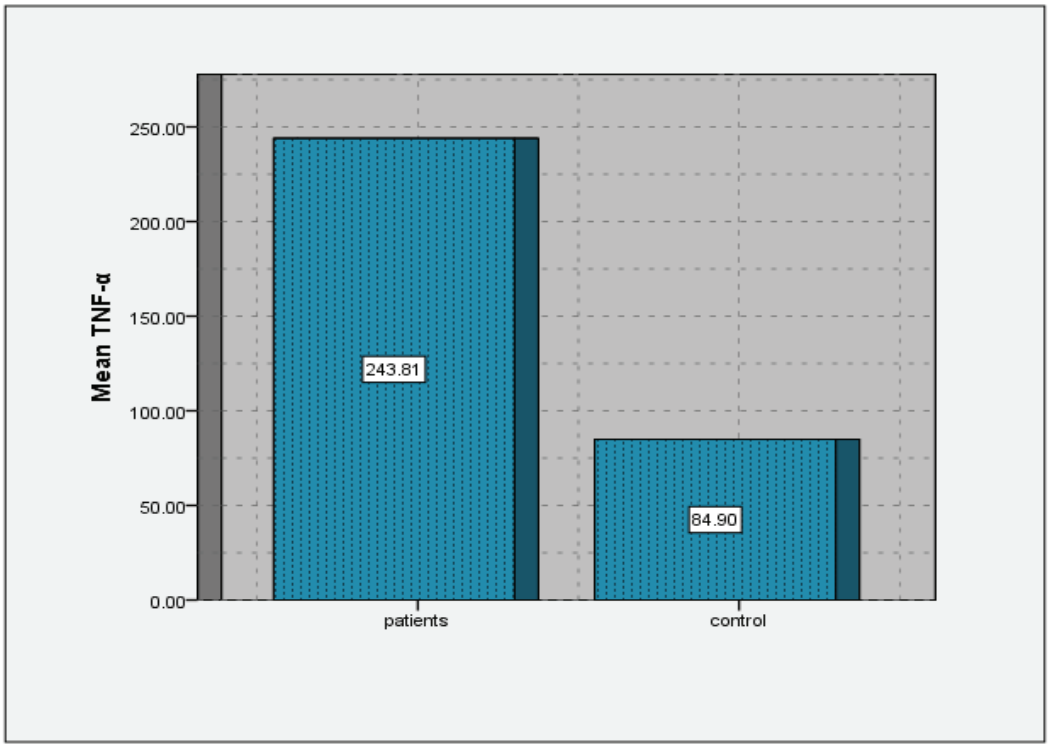

Figure 2: TNF-α levels in renal failure patients and control.

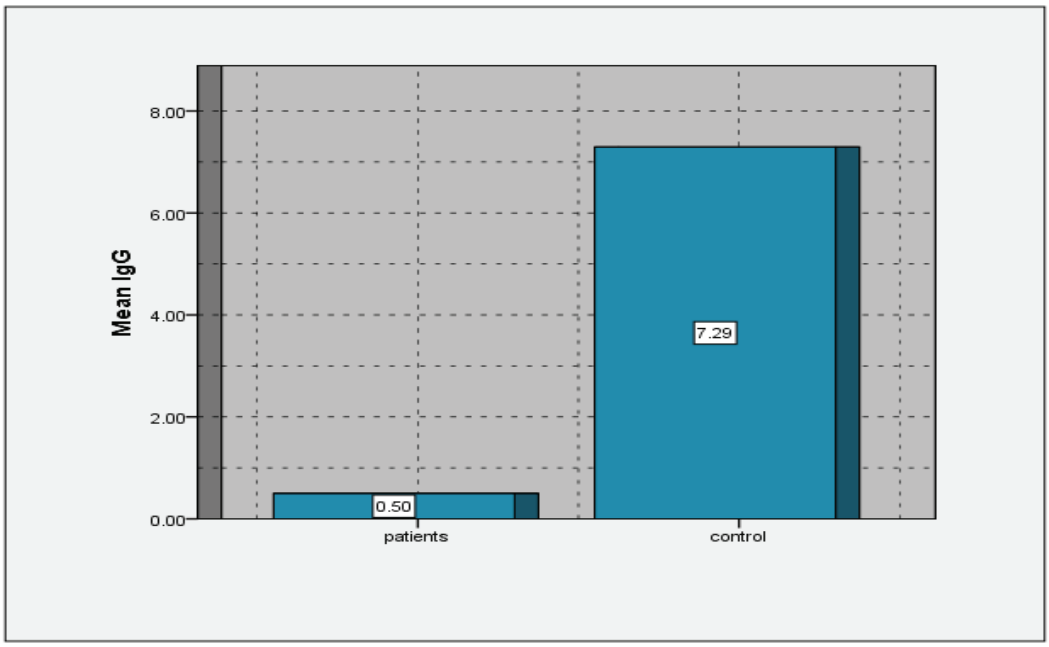

Figure 3: IgG levels in renal failure patients and control.

During immunologic study which dealt with important parameters such as KIM-1 molecules, pro-inflammatory TNF-α, IgG antibodies show all parameters levels was increased in Renal failure patients serum except the level of antibodies that indicated the patients have immune response against disease lead to induced pro-inflammatory cytokines in the end stage of disease and decrease the level of antibodies which may increase in early stage of disease and return to decline. Immune detection of KIM-1 found high levels in serum and urine by the sandwich ELISA technique. All aspects of inflammation and immune function may be affected by the high levels of urea and metabolic wastes, including a decrease in humeral and cell-mediated immunity, and defective phagocyte function. inflammatory response mediated by TNF-α response causes from persons who are

receiving dialysis, vascular access devices are common portals of entry for pathogens [17]. increase levels TNF-α were more common and associated with decrease levels of kidney function [18]. In experimental models refer that TNF-α causes direct kidney injury, TNF-α molecules may mediate glomerular injury by promoting an influx of immune cells such as macrophages and monocytes, induced proliferation of mesangial cells, and facilitating fibrosis in kidney [19]. The results demonstrated a significant decrease in **serum** total protein and in patients with kidney failure compared to healthy individuals [20] research showed that antibodies such as IgG, production by plasma cells from patients with kidney failure was lower than those produced by B cells from normal individuals. This founds demonstrated decrease humeral immune response in patients with renal failure [21].

Hematologic study of renal failure patients:

Current study dependent on hematological data collected by mean (CBC tests) which give picture to WBC, RBC, Platelets numbers in blood was score different in some blood variables this variations have significant statically at (<0.05) was appeared in (LYM., MON., GRA., RBC., HGB., HCT., MCV, MPV.) testing there are different between patients and control which recorded (1.06±0.42, 0.64±0.38, 3.62±1.04, 3.04±0.78, 8.33±1.84, 24.72±5.44, 85.06±8.29, 8.48±0.49) respectively compare with control (4.81±1.11, 0.40±0.18, 5.42±1.14, 4.02±0.46, 14.93±1.45, 33.64±3.58, 9.22±1.10) respectively at *p.* value (0.00) lower (<0.05). While remain tests have not significant statically between patients and control such as (WBC, MHC, MCHC, RDWS, RDWS, PLT, PCT, PDWS, PDWS, PLCC, PL-CR) tests.

As a routine tests can be using to all patients with renal failure to find out how the disease effect on another blood criteria, so that all patients take all blood films. During this study the results showed higher percent of patients have anemia by decline in RBC numbers and hemoglobin level. Patients with end-stage renal disease can suffer from anemia [22]. Results reported that anemia can develop well before the onset of uremic symptoms due to renal failure, and red blood cells production [23]. The defect in red blood cell production is affected by several factors such as the inability of kidneys to secrete erythropoietin hormone. In addition, other factors associated with renal failure, such as the accumulation of uremic toxins which play a role in inhibition bone marrow function [24]. In patients receiving dialysis blood loss resulting from loss of blood in the dialysis tubing and dialyzer after each hemodialysis treatment may also contribute to decrease Hb rate in blood [25]. Laboratory results refer that patients with renal disease show a variety of changes in hematological parameters [26]. The RBCs count, Hb and HCT levels in these patients, although often within the normal range, were significantly lower when compared to their levels in healthy controls the fall in white blood cells (WBC) that occur during hemodialysis may be attributed to the different dialysis membranes and sterilization methods employed [27]. However, indicated that the decreased RBC production by the bone marrow can attributed to iron deficiency, [28].

Conclusion

Increase kidney injury and inflammatory in serum patients with disease, by measured some parameters levels in sera as indicators for disease progression and decrease in some antibodies such as IgG concentration of in sera, as well as the hematologic tests referrer to disease may associated with anemia.

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

Conflict of Interest: Non

Funding: Non

References

1- Levy E.M., Viscose C.M., Horwitz R.I. The effect of acute renal failure on mortality: A cohort analysis. *Journal of the American Medical Association* 1996, 275, 1489–1494.

2- Thadhani R., Pascual M., Bonventre J.V. Acute renal failure. *New England Journal of Medicine* 1996, 334, 1448–1460.

3- Cotran R.S., Kumar V., Collins T. *Robbins pathologic basis of disease* 1999, 6th ed., pp. 932–933, 969–971, 1229, Philadelphia: W.B.Saunders.

4- Gerlach A.T., Pickworth K.K. Contrast medium-induced nephrotoxicity: Pathophysiology and prevention. *Pharmacotherapy* 2000, 20, 540–548.

5- National Institute for Health and Care Excellence. *Acute kidney injury: NICE clinical guideline 169*. London: NICE; 2013.

6- Haase M, Kellum JA, Ronco C. Subclinical AKI – an emerging syndrome with important consequences. Nat Rev Nephrol 2012;8:735-9.

7- Bragadottir G, Redfors B, Ricksten SE. Assessing glomerular filtration rate (GFR) in critically ill patients with acute kidney injury – true GFR versus urinary creatinine clearance and estimating equations. Crit Care 2013;17:R108.

8- Alvelos M, Lourenco P, Dias C, Amorim M, Rema J, Leite AB, Guimaraes JT, Almeida P, Bettencourt P. Prognostic value of neutrophil gelatinase-associated lipocalin in acute heart failure. Int J Cardiol; 2013, 165:51–55.

9- Lewington, A., & Kanagasundaram, S. Acute kidney injury. Retrieved fromwww.renal.org/guidelines/modules/acute-kidney-injury. 2011.

10- Ho KM, Power BM. Benefits and risks of furosemide in acute kidney injury. Anaesthesia 2010;65:283-93.

11- Hoste EA, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. Intensive Care Med 2015;41:1411-23.

12- Lewis, S.M. ; Bain, B.J. and Bates, I.. Dacie and Lewis practical hematology. 19th ed. *Churchill livingstone*. 2001, 1-5.

13- Abdel-Rahman EM, Okusa M.D. *Effects of aging on renalfunction and regenerative capacity*. Nephron Clin Pract; 2014, 127:15-20.

14- Nitta K, Okada K, Yanai M. *Aging and chronic kidney disease*. Kidney Blood Press Res; 2013, 38:109-20.

15- Ferrari P, Xiao J, Ukich A. Estimation of glomerular filtration rate: does haemoglobin discriminate between ageing and true CKD? Nephrol Dial Transplant; 2009, 24:1828-33.

16- Wesson, LG Renal hemodynamics in physiological states. In: Wesson LG, ed. Physiology of the Human Kidney. New York, NY: Grune & Stratton, 2017, pp. 96-108.

17- Lin F.; Zhang P.L.; Yang X.J.; Shi J.; Blasick T.; Han W.K.; Wang H.L.; Shen S.S.; Teh B.T.; Bonventre J.V. Human kidney injury molecule-1 (hKIM-1): a useful immunohistochemical marker for diagnosing renal cell carcinoma and ovarian clear cell carcinoma. Am J Surg Pathol 2007, 31, 371-81.

18- KARKAR AM, SMITH J, PUSEY C. Prevention and treatment of experimental crescentic glomerulonephritis by blocking tumor necrosis factor-alpha. *Nephrol Dial Transplant* 2001, 16:518–524,.

19- Inaoki, M. ; Sato, S. and Takehara, K. Elevated expression of CD23 on peripheral blood B lymphocytes from patients with bullous pemphigoid: correlation with increased serum IgE.J Dermatol Sci 2004, 35: 53-59.

20- Janssen, U. Bahlmann, F. Kohl, J Activation of the acute phase response and complement C3 in patients with IgA nephropathy.*Am J Kidney Dis* 2000, 35:21–28,.

21- Sarnak, M. Poindexter, A. Wang, S.R. Serum C-reactive protein and leptin as predictors of kidney disease progression in the Modification of Diet in Renal Disease Study. *Kidney Int* 2002, 62:2208–2215.

22- Mettang, T. ; Fritz, P. and Weber, J.; Uremic pruritus in patients on hemodialysis or continuous ambulatory peritoneal dialysis (CAPD). The role of plasma histamine and skin mast cells.Clin Nephrol, 2012, 34: 136-141.

23- Jeffrey, S. ; Berns, M.D.; Gary ,C.; and Alice, M.. Patient information: Chronic kidney disease. 2011.

24- Daugirdas, J.T.; Black, P.G. and Ing, T.S. "Handbook of Dialysis" (4thedn), Lippincott Williams & Wilkins, a Wolters Kluwer Business, Philadelphia. 2007.

25- Mohamed, A. ; Babiker, M. A. ; Merghani, L. B. and Abdulmajeed, M. H.. Hematological changes post-hemo and peritoneal dialysis among renal failure patients in Sudan.Saudi J Kidney Dis Transpl 2008, 19: 274-279.

26- Ho, C. H.; Chau, W. K. ; and Hsu, H. C. . Predictive risk factors and prevalence of malignancy in patients with iron deficiency anemia in Taiwan. Am J Hematol 2005, 78: 108-112.

27- Anding, K. Gross, P. Rost, J. M. and Allgaier, D. The influence of uraemia and haemodialysis on neutrophil phagocytosis and antimicrobial killing. Nephrol Dial Transplant 2003, 18: 2067-2073.

28- Nariman, Z.; Iman, W.; Azza, S. and Manal, Z.. Granulocyte Macrophage Colony Stimulating Factor Mediated Modulation of Polymorphonuclear Leukocyte Dysfunction in Chronic Kidney Disease and Hemodialysis Patients. Journal of American Science 2012, 8: 731-737.