Research Article

Effect of Hepatitis "C" Virus Infection on Hemoglobin Level and Iron Profile in Chronic Hemodialysis Patients in El-Minia Governorate

Mohamed I. Atta*, Ashraf M. Genina* and Reda H. Tawfiek**
* Department of internal Medicine & Nephrology, Beni-sueif University
** MBBch. Ain Shams University

Abstract
Hepatitis c virus (HCV) infection is a major health trouble worldwide. HCV is not only the causative of kidney disease but also contributes to increase morbidity and mortality in patients with established CKD. The current study was carried out at El-Minia governate. These observational, analytic and longitudinal study was carried out on ١٤٣٣ patients with chronic kidney disease on regular haemodialysis. Participants divided into two groups according to HCV surface antibody by ELISA test. All patients underwent a thorough clinical evaluation (full history taking, general examination and systemic examination). The laboratory tests to all individuals were recorded from their files including: Hepatitis C virus markers and iron profile (serum iron, serum ferritin, total iron binding capacity and transferring saturation). The aim of this study was to reveal the effect of HCV infection on the hemoglobin level, iron profile and EPO dose in chronic renal failure patients under regular haemodialysis in El-Minia Governorate. Results of our study can be discussed as follows; both haemoglobin levels and haematocrit values were significantly higher in hepatitis C virus positive compared with its corresponding one from the negative group. **Aim of work;** The aim of this study is to reveal the effect of HCV infection on the hemoglobin level, iron profile and EPO dose in chronic renal failure patients under regular haemodialysis in El-Minia Governorate.
Key words: Hemodialysis, hepatitis C, Iron Profile

Introduction
Hepatitis C virus (HCV) infection is the most common cause of chronic hepatitis in hemodialysis patients (Mathurin et al., ١٩٩٩). HCV infection may increase the risk of death in the hemodialysis population. Patients with end-stage renal disease are at risk of acquiring HCV infection from blood product transfusion, organ donor or from other hemodialysis patients. The prevalence of anti-HCV antibodies in different countries using enzyme linked immune-sorbent assay (ELISA) among dialysis patients was ٨-٣٦٪ in North America, ٣٩٪ in South America, ١-٥٤٪ in Europe, ١٧-٥١٪ in Asia. The advent of second-generation tests has revealed an even higher prevalence of anti-HCV antibodies in hemodialysis patients (Pereira, ١٩٩٨). Caramelo et al., ١٩٩٦ found that hepatitis C virus infected hemodialysis patients need lower erythropoietin (EPO) and iron supplementation compared to non-infected hemodialysis patients. Biochemical markers of iron overload are very common in patients with chronic hepatitis C, increase in serum iron is present in ٣٦٪, transferring saturation in ١٨-٣١٪ and serum ferritin in ٣٠-٥٥٪. Kurihara and Saito ١٩٩٨ reported that EPO should be used together with parenteral iron administration, even in HCV-Positive patients, because it is safe at low doses under careful observation. It is well recognized that the parenteral iron administration is recommended for hemodialysis patients treated with -EPO. On the other hand, hepatic iron concentration increases in chronic hepatitis C, and iron reduction improves serum transaminase levels in these patients (Kurihara and Saito, ١٩٩٨). Spontaneous erythropoietin production was reported in end-stage renal disease patients with hepatitis virus infection (Browne et al., ١٩٨٧, Mathurin et al., ١٩٩٩). Sahin et al., ٢٠٠٣ have reported higher levels of hemoglobin in hepatitis C

positive hemodialysis patients compared to hepatitis C negative hemodialysis patients.

Patients and Methods

Subjects:

This observational, analytic and longitudinal study was carried out on ١٤٣٣ ESRD patients undergoing HD in different districts of EL MINIA Governorate in the period from December ٢٠١٤ to May ٢٠١٥. Exclusion criteria included patients with HBsAg or HIV ab positive, malignancy like renal cell carcinoma or cryoglobulinemia, gastrointestinal bleeding, treatment with interferon and/or ribavirin, patients with non-renal cause of anemia other than iron deficiency, haemopoietic disorders (e.g. multiple myeloma), pregnancy, patients with inflammation, or with debilitated diseases like tuberculosis, and decompensated liver disease. the study design was explained to all participants. All hemodialysis patients were interviewed and subjected to full history taking, and careful review of all available medical records. The data were collected to a hard follow up sheet (questionnaire form) done specifically for the study and had been used to address the following points; age, sex, cause of chronic kidny disease, duration of hemodialysis, viral status at start of hemodialysis included HCV-antibodies and HBsAg, history of seroconversion and time of its occurrence, duration before seroconversion, history of blood transfusion, history of surgical operations, family history of hepatitis, switch of patients between different dialysis centers, infection control measures in the centers, isolation procedures, history of bilharziasis, venous access, and anaemic status. Special focusing was done for recording the following laboratory investigations; hepatitis C virus markers: HCV antibody by ELISA method, hepatitis B virus markers: HBs antigen by ELISA method, complete blood count, haemoglobin level by ERMA INC, PCE-٢١٠ N device, serum ferritin by ELISA method (R&D), and transferrin saturation: serum iron / total iron binding capacity x ١٠٠. We diagnose anemia in adults and children >١٥ years with CKD when the Hb concentration is <١٣.٠ g/dl (<١٣٠ g/l) in males and <١٢.٠ g/dl (<١٢٠ g/l) in females.

Results

El-Minia Governorate is one of the Upper Egypt's Governorates, about ٢٣٤ kilometres to the south of Cairo, it comprises nine districts, its population was ٥٤٠٥٣٥٣ populations according to the records of the Egyptian Ministry of Health and population and the Central Agency of Egypt for public mobilization & Statistics ٢٠١٥. In El Minia governorate, there are ١٧٠٠ ESRD patients on regular haemodialysis. Patients who agreed to participate on our study are ١٤٣٣ (٨٤.٣٪), aged from ١٣-٩٣ years with average ٥١.٦ ±١٣.٧ years. ٩٧٢ from them are males (٦٧.٨٪) & ٤٦١ are females (٣٢.٢٪). ٧٩.٩٪ are rural while ٢٠.١٪ are urbans. Nonsmokers were higher with percentage ٦١.٥٪ than smokers with percentage ١٤٪ & ex-smokers ٢٤.٥٪ (table ١).

Table ٢ shows that hypertension is the most common cause of ESRD with percentage ٣٢.٠٣٪ and ٢٦.٨٧٪ are of unknown causes. While obstructive uropathy, DM and glomerulonephritis occupying percentage ١٥.١٤٪, ١١.٤٪ and ٩.١٤٪ respectively. Other uncommon causes as polycystic kidney, analgesic nephropathy, bilhariziasis and SLE occupying lower percentages. Fig. ١ show that ٣١.١٪ of the patients were in El-Minia city (the capital of El Minia governorate) as it contains ٤ units so the main bulk of patients present in it, ١٢.٦ % of the patients were in Abo-Korkas and ١٢.٤٪ of the patients were in Mallawi. As regard virus status of HD patients in our study, the prevalence of HCV infection was ٧٤٤ (٥٢٪) including ١٩٩ with seroconversion, out of ١٤٣٣ patients HCV antibodies were negative in ٦٨٩ (٤٨٪), ١.٤٪ were positive HBsAg (fig ٢).

Table ٣ shows that number of patients undergoes laboratory investigation widely variant; Hb level, Creatinine and urea before dialysis were the most common laboratory investigations done to HD patients in El-Minia governorate. From ١٤٣٣ patients, only ٢٩١ (٢٠.٣٪) patients from ٣ hospitals how do iron profile investigations in the form of: serum iron, TIBC & serum ferritin. Those ٢٩١ patients are considered our patient group. Hb levels in all the ٢٩١ patients were low and varied from ٥.٣ – ١٢

gm\dl (main ± SD ١٠.٣±٢.٣ gm/dl), serum iron level varies from ٣٤ – ٢٣٨ ug/dl (main ± SD ١٢٣.٥±٣٧.٧ ug/dl), TIBC varies from ٩٩ – ٥٤٩ ug/dl (main ± SD ٢٦٨.٩±٨٤.٧ ug/dl) and ferritin varies from ١٢٨ - ٤٥٤٣.٢ ng/ml (main ± SD ٢٥٠٧.٣±٣٠٠٠.٦ ng\ml) (Table ٤). Out of these ٢٩١ patients, ١٨٤ patients were positive to HCV antibodies and ١٠٧ patients were negative with upper hand to male patients (Table ٥).

Table ٦ shows a comparison between HCV positive and HCV negative hemodialysis patients in this group. HCV positive patients had statistically significant higher hemoglobin levels (main ±SD ١١.٥ ± ١.٨ gm/dl, p < ٠.٠٠١), and serum iron (main ±SD ١٢٨.٧±٣٩.٤ ug/dl, p< ٠.٠٠٢) than HCV negative patients. There was no statistically significant deference between the ٢ groups as regard TIBC or serum ferritin & gender. As regard the erythropoetin and intravenous iron doses, the HCV positive group received lower doses than HCV negative group but this was not statistically significant (Table ٦). We subdivide this group according to the locality to three groups; Group A (Samalot hospital; ٢٩ males & ١٤ females), Group B (Maghagha hospital; ٥٩ males & ٤١ females) and Group C (Beni Mazar hospital; ١٠٣ males & ٤٥ females) (Table ٧). From these groups, there are ١٨٤ HCV +ve & ١٠٧ –ve patients classified as; Group A (٢٤ +ve, ٥ -ve males / ٥ +ve, ٩ –ve females), Group B (٣١ +ve, ٢٨ –ve males / ٢٤ +ve, ١٧ –ve females), and Group C (٦٩ +ve, ٣٤ –ve males / ٣١ +ve, ١٤ –ve females) (Table ٧).

Table ٧ shows that patients in Maghagha have statistically significant lower Hb level (٩.٩±٢.١gm/dl) than patients in Beni_Mazar (١٠.٦±٢.٥gm/dl) ($P_٣$=٠.٠١٦), while there was no statistically significant difference between other groups as regard Hb level. All the ٣ groups had high serum iron levels but still within normal ranges, and normal levels of total iron binding capacity but had severely elevated serum ferritin levels. Table ٨ shows that there is a highly statistically significant deference between HCV +ve &-ve patients in Samalot hospital as regarding HB & ferritin as the HCV -ve patients had lower HB (٨.٥±١.٣ gm/dl) and lower serum ferritin level (١٨٩٣.٩±١٦٩٠.١ ng/ml), but there was no statistically significant deference between them as regard S.iron & TIBC. Table ٩ shows that there is a highly statistically significant deference between HCV +ve &-ve patients in Maghagha hospital as regarding HB, iron & ferritin as the HCV -ve patient had lower levels (٨.٣±١.٤ gm/dl, ١٠٥.٨±٣٠.٩ ug/dl, ١٠٢١.٤±٤٧٩.٩ ng/ml respectively) than HCV +ve patients, while no statistically significant deference between them as regard TIBC. Table ١٠ shows that there is a highly statistically significant deference between HCV +ve &-ve patients in Beni_Mazar hospital as regarding HB (lower in HCV -ve patients ٨.٢±١.٤ gm/dl), and there was a statistically significant deference between them as regard TIBC (higher in HCV -ve patients ٣١٨.٤±٨١.٦ ug/dl), while there was no statistically significant deference as regard S. iron & ferritin.

Table (١): General characteristics of all ESRD patients (N = ١٤٣٣)

Baseline characteristics		
Age (years)	**Range (years)**	١٣ – ٩٣
	Mean ± SD	٥١.٦ ± ١٣.٧
Sex	**Male**	٩٧١ (٦٧.٨٪)
	Female	٤٦٢ (٣٢.٢٪)
Residence	**Urban**	٢٨٨ (٢٠.١٪)
	Rural	١١٤٥ (٧٩.٩٪)
HCV antibodies	**Positive**	٧٤٤ (٥١.٩٪)
	Negative	٦٨٧(٤٨.١٪)
Smoking	**Smoker**	٢٠٠ (١٤٪)
	Non-smoker	٨٨١ (٦١.٥٪)
	Ex-smokers	٣٥٢ (٢٤.٦٪)

Table (٢): Causes of renal failure among dialysis patients of Minia governorate (N=١٤٣٣)

Causes of renal failure	Number	Percent
Hypertensive nephropathy	٤٥٩	٣٢.٠٣٪
Diabetic nephropathy	١٦٣	١١.٤٪
Glomerulonephritis	١٣١	٩.١٤٪
Obstructive uropathy	٢١٧	١٥.١٤٪
Analgesic nephropathy	٢٠	١.٣٩٪
Polycystic kidney	٢٨	١.٩٥٪
Unknown cause	٣٨٥	٢٦.٨٧٪
Bilharziasis	٧	٠.٤٩٪
Systemic Lupus Erythrematosis	٧	٠.٤٩٪
Other causes	١٦	١.١٢٪
Total	١٤٣٣	١٠٠٪

Fig. ١: Prevalence of ESRD in different districts of Minia Governorate ٢٠١٥

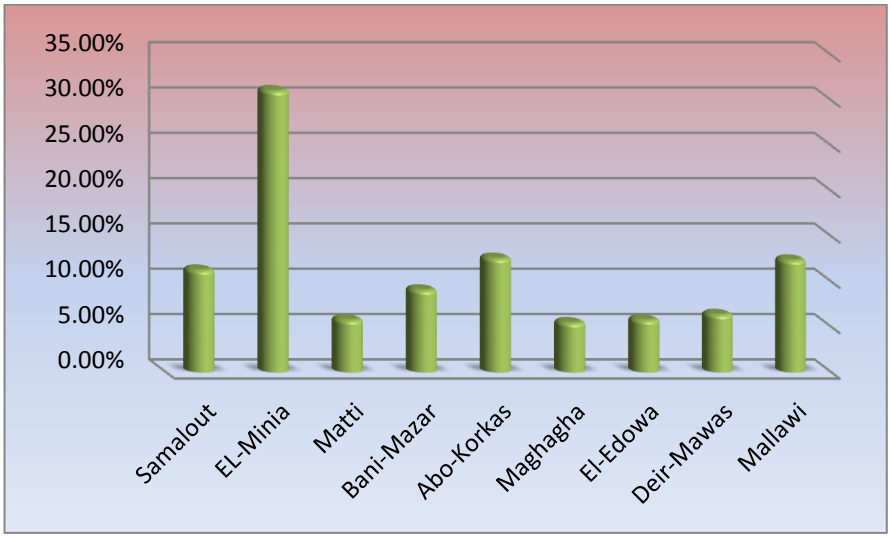


Fig (٢): Viral status in all ESRD patients

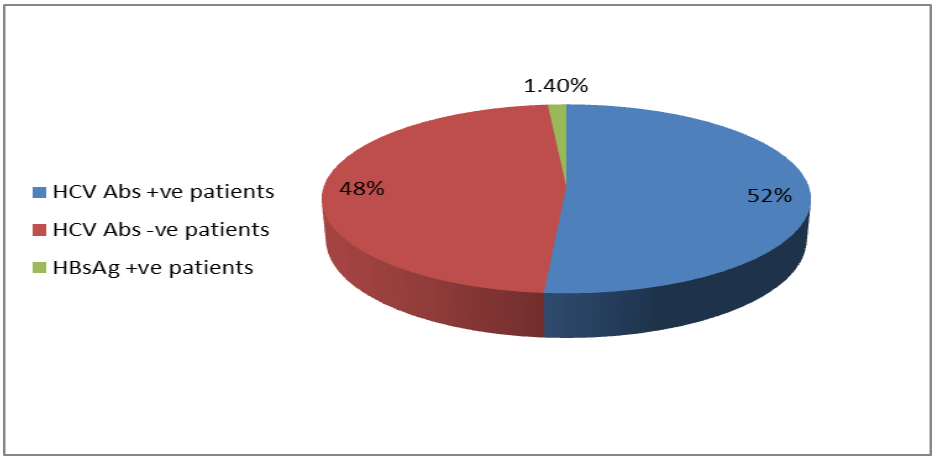


Table (٣): Laboratory data of all ESRD patients

Laboratory data	Number	Range	Mean ± SD
Urea before dialysis	١٣٦٥	٩٠ – ٣٢٠	١٤٤.٢ ± ٤٢.٨
Urea after dialysis	٣٠٨	٥٠ – ١٨٦	٧٠.٦ ± ٢٢.٦
Creatinine	١٣٦٤	٢.٥–١٧.٣	٧.٣ ± ٣.١٤
HB	١٤٣٢	٤.٢ – ١٢	٩.٥ ± ١.٨
Serum iron	٢٩١	٣٤– ٢٣٨	١٢٣.٥ ±٣٧.٧
TIBC	٢٩١	٩٩ – ٥٩٤	٢٦٨.٩ ± ٨٤.٧
Feritin	٢٩١	١٢٨–٤٥٤٣.٢	٢٥٠٧.٣ ± ٣٠٠٠.٦

Table (٤): Hemoglobin and iron profile of the study group (n=٢٩١)

		Patients
Hemoglobin	**Range** **Mean±SD**	٥.٣-١٢ gm/dl ١٠.٣±٢.٣ gm/dl
Iron	**Range** **Mean±SD**	٣٤-٢٣٨ ug/dl ١٢٣.٥±٣٧.٧ ug/dl
TIBC	**Range** **Mean±SD**	٩٩-٥٤٩ ug/dl ٢٦٨.٩±٨٤.٧ ug/dl
Ferritin	**Range** **Mean±SD**	١٢٨-٤٥٤٣.٢ ng\ml ٢٥٠٧.٣±٣٠٠٠.٦ ng\ml

SD: Standard deviation

Table (٥): HCV and gender in the study group (n=٢٩١)

	Patients
HCV	
• Positive	١٨٤ (٦٣.٢%)
• Negative	١٠٧ (٣٦.٨%)
Gender	
• Male	١٩١ (٦٥.٦%)
• Female	١٠٠ (٣٤.٤%)

Table (٦): Comparison between HCV positive and negative patients in the study group

	Positive (n=١٨٤)	Negative (n=١٠٧)	P-value	Sig.
Gender	M: ١٢٤ (٦٧.٤٪) F: ٦٠ (٣٢.٦٪)	M: ٦٧(٦٢.٦٪) F: ٤٠(٣٧.٤٪)	٠.٢٤٢	NS
Hemoglobin Mean±SD	١١.٥±١.٨	٨.٣±١.٤	٠.٠٠١	HS
Iron Mean±SD	١٢٨.٧±٣٩.٤	١١٤.٥±٣٢.٨	٠.٠٠٢	HS
TIBC Mean±SD	٢٦٤.٢±٨٤.٩	٢٧٧±٨٤.١	٠.٢١٣	NS
Ferritin Mean±SD	٢٦٢١.٧±١٦٧٤.٩	٢٣١٠.٧±٤٤٤١.٦	٠.٣٩٥	NS
EPO ١٠٠٠ IU monthly dose	١٠ ± ٢.١	١٢ ± ٢.٤	٠.٣١٥	NS
IV iron ١٠٠mg monthly dose	٣ ± ١.٢	٤ ± ١.٥	٠.١٣٥	NS

Table (٧): Comparison between ESRD patients in Samalot, Maghagha & Beni-Mazar

	Group A (n=٤٣)	Group B (n=١٠٠)	Group C (n=١٤٨)	P value	Sig.
Gender	M:٢٩ F:١٤	M:٥٩ F:٤١	M:١٠٣ F:٤٥		
HCV	+ve M:٢٤ +ve F:٥ -ve M:٥ -ve F:٩	+ve M:٣١ +ve F:٢٤ -ve M:٢٨ -ve F:١٧	+ve M:٦٩ +ve F:٣١ -ve M:٣٤ -ve F:١٤		
Hemoglobin Range Mean±SD	٦.٧-١١.٥ ١٠.١±١.٧	٥.٣-١٢ ٩.٩±٢.١	٥.٩-١٢ ١٠.٦±٢.٥	P١=٠.٦٤٥ P٢=٠.١٨٤ P٣=٠.٠١٦	NS NS S
Iron Range Mean±SD	٣٤-٢٠٩ ١٢٣.٧±٤٩.٠	٥٣-٢٣٨ ١٢٤.٨±٤١.٠	٦٠-١٩٨ ١٢٢.٦±٣١.٣	P١=٠.٨٧٣ P٢=٠.٨٧٣ P٣=٠.٦٦٠	NS NS NS
TIBC Range Mean±SD	٩٩-٣٨٠ ٢٤١.٣±٦٨.٢	١١٤-٤٣٨ ٢٤٣.٢±٧٢.٣	١٢٣-٥٤٩ ٢٩٤.٣±٨٩.٣	P١=٠.٨٩٦ P٢=٠.٠٠١ P٣=٠.٠٠١	NS HS HS
Ferritin Range Mean±SD	١٢٨-٧٣٦٩ ٣١٢٥.٧±٢١٧٦.٣	٣٢٠-٦٥٩٠ ١٦٢٠.٣±١٣٠٨.٣	٧٦٢-٤٥٤٣٢ ٢٩٢٧.٠±٣٧٩٩.٠	P١=٠.٠٠٥ P٢=٠.٦٩٧ P٣=٠.٠٠١	HS NS HS

P١: Comparison between group A and group B, P٢: Comparison between group A and group C, P٣: Comparison between group B and group C, S: P-value < ٠.٠٥ (Significant), HS: P-value < ٠.٠١ (High significant), P-value > ٠.٠٥ (Non-significant)

Table (٨): Comparison between HCV positive and negative patients in Samalot (group A):

	Positive (n=٢٩)	Negative (n=١٤)	P value	Sig.
Hemoglobin Mean±SD	١٠.٩±١.٣	٨.٥±١.٣	٠.٠٠١	HS
Iron Mean±SD	١٢٨.٢±٥٠.٤	١١٤.٣±٤٦.٣	٠.٣٨٩	NS
TIBC Mean±SD	٢٣٨.٣±٥٤.٦	٢٤٧.٤±٩٢.٦	٠.٦٨٦	NS
Ferritin Mean±SD	٣٧٢٠.٤±٢١٥٧.٢	١٨٩٣.٩±١٦٩٠.١	٠.٠٠٨	HS

Table (٩): Comparison between HCV positive and negative patients in Maghagha (group B):

	Positive (n=٥٥)	Negative (n=٤٥)	P value	Sig.
Hemoglobin Mean±SD	١١.٢±١.٧	٨.٣±١.٤	٠.٠٠١	HS
Iron Mean±SD	١٤٠.٣±٤١.٩	١٠٥.٨±٣٠.٩	٠.٠٠١	HS
TIBC Mean±SD	٢٤٤.٢±٧٩.٤	٢٤٢.٠٢±٦٣.٣	٠.٨٨٣	NS
Ferritin Mean±SD	٢١١٠.٤±١٥٥١.٤	١٠٢١.٤±٤٧٩.٩	٠.٠٠١	HS

Table (١٠): Comparison between HCV positive and negative patients in Beni_Mazar (group C):

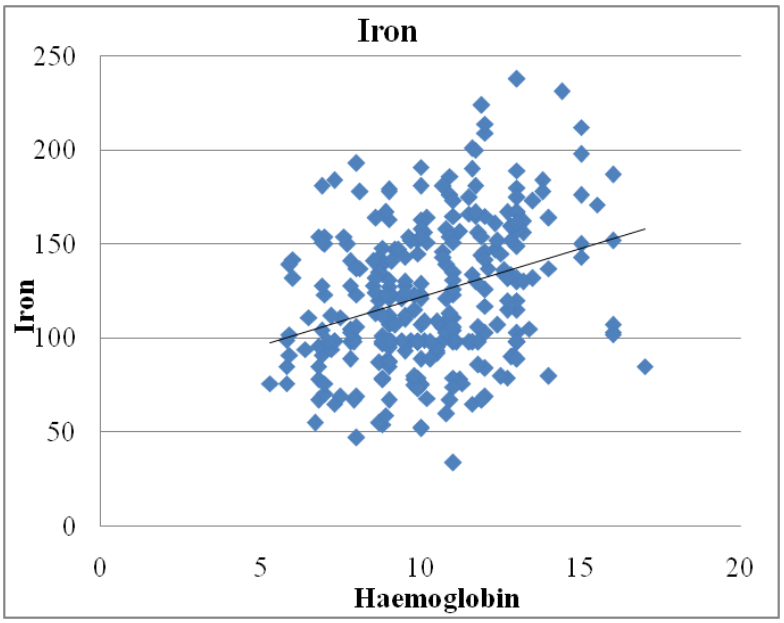
	Positive (n=١٠٠)	Negative (n=٤٨)	P value	Sig.
Hemoglobin Mean±SD	١١.٨±١.٩	٨.٢±١.٤	٠.٠٠١	HS
Iron Mean±SD	١٢٢.٦±٣٢.٨	١٢٢.٧±٢٨.١	٠.٩٧٨	NS
TIBC Mean±SD	٢٨٢.٧±٩٠.٩	٣١٨.٤±٨١.٦	٠.٠٢٢	S
Ferritin Mean±SD	٢٥٨٤.٣±١٤٣٤.١	٣٦٤٠.٩±٦٣٢٧.٤	٠.١١٣	NS

Table (١١): Correlation between Hemoglobin and other parameters in the study group

		Hemoglobin
Iron	**r**	**٠.٣١٥**
	Sig.	**٠.٠٠١****
TIBC	**r**	٠.٠٣٩
	Sig.	٠.٥٠٧
Ferritin	**r**	٠.١٠٢
	Sig.	٠.٠٨٣

r: Correlation coefficient

Figure (٣) Correlation between hemoglobin and iron



Discussion

HCV infection causes significant morbidity and mortality in patients with end-stage renal disease on hemodialysis. The prevalence of anti-HCV antibody is higher in patients on hemodialysis than in healthy populations. Several risk factors contributing to this high prevalence of HCV infection have been identified, and include the number of blood transfusions, duration of end-stage renal disease, mode of dialysis, and prevalence of HCV infection in the dialysis unit**.** It has been reported that the duration of hemodialysis is significantly longer in anti-HCV-positive patients than in anti-HCV-negative patients. Further, it has been observed that patients on hemodialysis for more than ١٠ years have an increased incidence of HCV infection. The risk of acquiring HCV infection on hemodialysis is estimated at approximately ١٠٪ per year (Pereira et al., ١٩٩٨). HCV infection remains a major health problem that can cause substantial liver-related morbidity and mortality in patients with end stage renal disease (Liu CH et al., ٢٠١١).

In Egypt, HCV infection has reached an epidemic level of prevalence. A high prevalence of HCV antibodies was reported among healthy blood donors and a much higher prevalence of HCV antibodies among patients with glomerulopathy (Sabry AA., et al., ٢٠٠٢). However, the effect of HCV infection on erythropoiesis has still not been fully elucidated. The aim of our study was to define further the effect of HCV infection on erythropoiesis in patients with end-stage renal disease through our patient population. The present work aimed to study the effect of HCV infection on hemoglobin level, iron profile and erythropoietin dose in chronic hemodialysis patients. It was conducted on ١٤٣٣ patients admitted at El_Minia gover-nrate. Analysis of the results revealed that there was no significant difference between group ١ (patients with chronic renal failure on regular haemodialysis with negative HCV antibody) versus group ٢ (patients with chronic renal failure on regular haemodialysis with positive HCV anti body) regarding age, gender, dialysis adequacy, serum creatinine and liver enzymes. Results from our study revealed that all patients had anemia (a haemoglobin level < ١٢ g/dl for all females and < ١٣ g/dl for males; based on WHO criteria). Anemia in patients of the present study was normocytic normo-chromic with adequate iron availability by parameters: TSAT (transferrin saturation) > ٢٠٪ and ferritin > ١٠٠ ng/ml suggesting that it is anemia of chronic kidney disease. Our study showed a significant higher haemoglobin level with positive HCV markers (group ٢) than patients with negative HCV markers (group ١) P Value =٠.٠٠١. In our study, not only hemodialysis patients with HCV infection tended to have higher mean hemoglobin than those without HCV infection, but also the average dose of erythropoetin required was lower in the anti-HCV-positive group than in the anti-HCV-negative group. Although the differences in erythropoetin dosage were not statistically significant, the mean values did follow a general trend which is in agreement with past reports of increased hemoglobin and hematocrit and decreased erythropoietin requirements in patients with liver injury.

Sahin et al., found that anti-HCV-positive patients with end-stage renal disease had higher hemoglobin and hematocrit levels than anti-HCV-negative patients (Sahin I et al., ٢٠٠٣). Similarly, Altintepe et al., concluded that anti-HCV positive patients on hemodialysis had higher serum erythropoietin levels and required less exogenous erythropoietin and iron than anti-HCV-negative patients (Altintepe L et al., ٢٠٠٤).

These results were in agreement with those of Khurana et al., (٢٠٠٨); they evaluated the effect of HCV infection on anemia in the haemodialysis population with an ٨-year retrospective case-control study. They concluded that patients with HCV infection had higher baseline haemoglobin and lower requirements of exogenous EPO replace-ment compared with their age-matched, gender matched and race-matched dialysis counterparts. There was no significant difference in intravenous iron need between the groups but there was a suggestive lower trend in the hepatitis group. Zumrutdal A, and sezgin N, ٢٠١٢ in a trial to explain these findings they reported that hepcidin is produced in the liver & it is a key regulator of iron haemostasis by blocking iron

absorption in the gut and iron release from macrophage & hepatocyte stores. It is filtered and degraded by the kidney. Hepcidin levels are elevated in patients with CKD; and thus, high hepcidin levels are thought to be linked to anemia of renal failure (Zumrutdal A, and sezgin N, ٢٠١٢). On the other hand, lower serum hepcidin levels were shown to be releated to the severity of liver fibrosis in chronic hepatitis patients without renal failure. Combining these data, we hypothesize that the probable lower serum hepcidin levels related with liver disease may have contributed to the improvement of anemia in haemodialysis patients. (Zumrutdal A, and sezgin N, ٢٠١٢).

Results of our study were also in agreement with Lin et al., (٢٠٠٨) and Alsaran et al., (٢٠٠٩) who investigated the influence of chronic hepatitis on anemia in haemo-dialysis patients. They both found that hemoglobin levels were significantly more elevated in the chronic hepatitis group of haemodialysis patients. Furthermore, Zumrutdal (٢٠١١) reported the same results.

They retrospectively compared the erythro-poietin-independent haemodialysis patients who had hepatitis with those who did not. Haemodialysis patients with or without hepatitis who could maintain nearly normal hemoglobin levels of ١٢ g/dl or over, without the administration of recombinant human erythropoietin for at least one year were analyzed retrospectively. They found that while ٨٪ of haemodialysis patients without hepatitis were able to maintain nearly normal hemoglobin levels (>١٢ g/dl) without the administration of recombinant human EPO, the corresponding ratio in haemodialysis patients with chronic hepatitis was greater than ٣-fold (٢٥.٣٪) (Zumrutdal A; ٢٠١١).

In contrast, these results disagreed with those of Sabry et al., (٢٠٠٧); who studied the effect of hepatitis C virus infection on hemoglobin levels in a retrospective case control study carried out with a total of ٩٩ subjects receiving chronic haemodialysis for at least one year. They reported that HCV-positive and HCV-negative chronic haemodialysis patients have comparable hemoglobin levels and the erythropoietin dose was not influential as its lower value in HCV-positive patients did not reach a statistically significant level (Sabry A., et al., ٢٠٠٧). Furthermore, Boubaker et al., (٢٠٠٩); evaluated the effect of HCV infection on anemia in haemodialysis patients, a total of ٥٧ haemodialysis patients not receiving any recombinant EPO therapy were included in the study. They reported no significant difference between HCV-positive and negative haemodialysis patients regarding mean hemoglobin levels. Our study revealed significant difference between HCV positive group versus HCV negative group regarding serum iron and hemoglobin levels being higher in HCV positive group. Ferritin is an acute phase reactant that is released from the liver with hepatic inflammation, and so HCV positive patients were expected to have higher ferritin compared with HCV negative patients, while our results detect that there was no significant deference between the two groups as regard serum ferritin levels.

Our results were also in agreement with those of Altintepe et al., (٢٠٠٤); who studied the influence of chronic HCV infection on EPO and iron requirement in haemodialysis patients in a prospective case-control study; ٤٩ HD patients were included, follow-up time ١ year for this study. They reported that Anti-HCV positive haemodialysis patients had higher serum endogenous EPO levels and required less EPO and iron replacement as compared to Anti-HCV negative patients. In either case, hepatonecrosis from inflammation from hepatitis or a regene-rating liver post injury could potentially result in release of EPO from hepatocytes into the circulation (Khurana A., et al., ٢٠٠٨). Red cell production in the body requires the presence of EPO and adequate iron stores. Erythropoietin is the major hormone required for red cell precursor proliferation in the bone marrow. It stimulates the blast forming units erythroid in the bone marrow to mature into pro-erythroblasts, which later form the circulating red cells. Its major site of production is the peri tubular fibroblasts in the kidney. Some degree of endogenous EPO production also comes from the liver (simon p et al., ١٩٨٠).

This has been found to be significant especially in the fetus and in nephrectomized animals in previous studies. The exact site of EPO production in the liver is not clear. Some studies have pointed it out to be located in the Kupffer cells (Gordon AS et al., ١٩٨٠) while others believe it to be within hepatocytes surrounding the central veins, along with contribution from the Ito cells in the space of Disse (Eckardt KU et al., ١٩٩٦). In either case, hepatonecrosis from inflammation from hepatitis or a regenerating liver post injury could potentially result in release of EPO from hepatocytes into the circulation.

The other major requirement for erythropoiesis is adequate iron stores. This is assessed mainly by calculating serum TSAT (serum iron/serum total iron binding capacity X١٠٠) and measuring circulating ferritin levels (because bone marrow biopsy to estimate iron stores is rarely performed). After dialysis therapy is initiated, almost all patients require periodic IV-iron supplementation to keep iron saturation in the range of ٢٠٪ to ٥٠٪and ferritin levels between ١٠٠ and ٨٠٠ ng/mL based on KDOQI guidelines. Patients with HCV tend to have higher ferritin compared with non-HCV patients, as ferritin is an acute phase reactant that is released from the liver with hepatic inflammation (Shan Y et al., ٢٠٠٥). Although this may be the case in those on dialysis population, the infusion of IV-iron on dialysis elevates the ferritin levels, even in non-HCV patients. We hypothesize that the chronic inflammation as a result of HCV infection or the increased production from the regenerating liver cells causes increased circulating EPO—causing improved hematocrit in these patients.

Conclusion

We concluded from this study that chronic kidney disease patients with positive HCV antibody tend to have higher haemoglobin and haematocrit levels than chronic kidney disease patients with negative HCV. The ferritin level also was high in positive than negative and consequently HCV positive patients required lower erythropoietin doses. Chronic inflammation of the liver may be the cause for increased EPO production, these needs to be clarified in further studies.

Recommendations

All patients with end-stage renal disease on regular hemodialysis should undergo regular investigations in the form of: iron study (serum iron, serum ferritin, TIBC), Hb level, HCV antibody & SGPT to optimize ESA dose. ESRD patients on RHD infected with hepatitis C virus may need a lower dose of erythropoiesis stimulating agent (ESA) therapy to reach the target haemoglobin level, this will be cost economic and to avoid hazards of ESA over dose such as thrombosis.

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