An-Najah National University

Faculty of Graduate Studies

Evaluation of anemia management among hemodialysis patients in Palestine: associated factors and clinical outcomes

By

Nada Sadek Rajabi

Supervisor

Dr. Samah Al-Jabi

This Thesis is Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Clinical Pharmacy, Faculty of Graduate Studies, An-Najah National University, Nablus, Palestine.

2020

Evaluation of anemia management among hemodialysis patients in Palestine: associated factors and clinical outcomes

By

Nada Sadek Rajabi

This Thesis was Defended Successfully on 23/1/2020 and approved by:

Defense Committee Members	**Signature**
1. Dr. Samah W. Al-Jabi / Supervisor	**……..…..…**
2. Dr. Hussein Hallak / External Examiner	**...……**
3. Dr. Rowa Al Ramahi / Internal Examiner	**…...……**

الاهداء

الى الداعم الصامد الذي لم يتنازل ولم يتوارى يوما عن تحقيق أحلامه فينا بكل ثبات وعزيمه، رمز التضحيه ... أبي الغالي

الى القلب الطيب الذي زرع الصدق والاخلاص في قلوبنا، الحضن الدافئ الذى افنى حياته في رعايتنا ..... أمي الحبيبه

الى روحي وأصدقاء طفولتي وأيامي ومشاركي ذكرياتي وعاهدي شبابي ومراه حياتي ..... أخواتي حياتي

الى سندي ورفيقي ..... أخي الحبيب

الى صديقاتي ورفاق دربي وداعمي أحلامي وصمودي

الى أساتذتي الأفاضل الذين اضاؤوا بعلمهم عقولنا

الى زملائي وزميلاتي الذين ساندوني ولم يدخروا جهدا في مساندتي

الى كل من رافقني وكل من ساهم في تحقيق هذا الانجاز

الشكر والتقدير

الحمد والشكر لله رب العالمين حمدا كثيرا طيبا مباركا فيه أن منّ علي من خيره الكثير وأنعم علي من فضله في العلم وأعانني على انجاز هذا العمل. الحمدلله عدد خلقه ورضى نفسه وزنة عرشه ومداد كلماته.

اتقدم بخالص الشكر والامتنان الى مشرفتي الدكتوره سماح الجابي لارشادها لي خلال دراستي العليا واعطائها لي فرصة العمل على هذا المشروع، كانت دائما ودوده ومتفانيه في دعمها لي.

ويسرني ان أتقدم بجزيل الشكر لكل الاساتذه والمشرفين الأفاضل في الصرح العلمي الكبير في قسم الصيدله السريرية في جامعه النجاح الوطنية.

وأود ان أتوجه بالشكر لوزاره الصحة الفلسطينية ومستشفى النجاح الوطني الجامعي بشكل عام وأقسام غسيل الكلى بشكل خاص لمساعدتي للوصول الى المعلومات اللازمه لهذا البحث.

ولكل من مد لي يد العون وساهم في انجاز هذا العمل له مني كل الشكر والتقدير.

الاقرار

انا الموقع ادناه مقدم الرسالة التي تحمل العنوان:

Evaluation of anemia management among hemodialysis patients in Palestine: associated factors and clinical outcomes

أقر بأن ما اشتملت عليه الرسالة هو من نتاج جهدي الخاص، باستثناء ما تمت الإشارة إليه حيثما ورد، وأن هذه الرسالة ككل أو أي جزء منها لم يقدم من قبل لنيل أي درجة أو لقب علمي أو بحثي لدى أي مؤسسة تعليمية أو بحثية أخرى.

Declaration

The work provides in the thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

اسم الطالب **Student's name:**

التوقيع **Signature:**

التاريخ **Date:**

List of content

List of Tables

List of Appendices

List of Symbols and Abbreviations

CBC	Complete Blood Count
CKD	Chronic Kidney Disease
CrCL	Creatinine Clearance
DM	Diabetes Mellitus
EGFR	Estimated Glomerular Filtration Rate
ESA	Erythropoietin Stimulating Agent
ESRD	End Stage Renal Disease
EQ-5D-5L	European Quality of Life- 5 Dimensions-5 levels
Hb	Hemoglobin
HD	Hemodialysis
HRQOL	Health Related Quality of Life
KDIGO	Kidney Disease: Improving Global Outcomes
NKF-KDOQI	National Kidney Foundation Kidney Disease/Dialysis Outcomes Quality Initiative
PD	Peritoneal Dialysis
RBC	Red Blood Cell
TSAT	Transferrin Saturation

Evaluation of anemia management among hemodialysis patients in Palestine: associated factors and clinical outcomes

By

Nada Sadek Rajabi

Supervisor

Dr. Samah Al-Jabi

Abstract

Background: Anemia is a frequent complication in patients on maintaining hemodialysis (HD). Appropriate management involves the administration of iron supplementation and erythropoietin stimulating agents (ESA) therapy besides monitoring the response. Poor health related quality of life (HRQOL) is also a common impairment in HD patients results from the dialysis procedure it-self or its related comorbidity. This study aimed to evaluate anemia management in HD patients from Palestine, determine the associated demographic and clinical characteristics with it, describe patients HRQOL and its association with appropriate anemia treatment.

Methods: The study was a cross sectional observational study; patients were included from three dialysis centers from West Bank - Palestine during the period of 24-June to 5-September 2018. The data filled by interviewing the enrolled patients and getting access to patient's health profiles. The data collection form consisted from two portions, the initial contains demographic and clinical information about the patients while the latest consists of the European Quality of Life 5- Dimensions scale (EQ-5D-5L) that represents the descriptive system and the EQ visual analogue scale (EQ-VAS) which represents the health status of patient in their own judgment.

Results: 226 patients included. Their mean age (± SD) was 57 ± 13.9 years. The mean hemoglobin (Hb) level (± SD) was 10.63 ± 1.71 g/dl, 34.1% of patients had Hb level 10-11.5 g/dl. Only 72.1% and 81.9% of patients recorded for serum ferritin and transferrin saturation (TSAT) respectively. 33.1% of patients had serum ferritin ≥ 500ng/ml and 50.3% had TSAT ≥ 30%. All patients who received iron supplementation received it by intravenous route and dose of 100mg of iron sucrose. Almost 86.7% of patients received Darbepoetin by intravenous route and weekly dose of 0.45 mcg/kg, 24% of them had Hb >11.5g/dl. On the other hand, 2.4% of patients had Hb < 10g/dl and did not received ESA therapy. Regarding EQ-5D-5L 22.6%, 54.9%, 32.3%, 29.6% and 25.2% of patients had level of "no problem" across the dimension of quality of life; mobility, self-care, usual activity, pain/ discomfort and anxiety respectively. Only 0.9% of patients had the highest degree of difficulty in the five dimensions. There was a significant association between Hb level, number of years the patients received HD and HRQOL.

Conclusion: Our study found a significant association between Hb level and patients HRQOL, therefore the appropriate management of anemia in HD patients by adherence to NKF-KDOQI guideline recommendations provides an improvement in their quality of life in addition to obtain the optimal therapy.

Key word: Anemia, Hemodialysis, Hemoglobin, Iron status, Erythropoietin stimulating agent, Health related quality of life.

Chapter one
Introduction

1.1 Background

Hemodialysis (HD) is the backbone and life sustaining therapy for patients with ESRD who cannot undergo renal transplantation (Murtagh et al., 2007, Levey and Coresh, 2012, Chauhan and Mendonca, 2015).

The overall stated number of patients with end stage renal disease (ESRD) undergoing HD in the West Bank of Palestine increased from 1014 in 2015 to 1119 patients in 2016, distributed in 12 units (Palestinian Ministry of Health, 2016, Palestinian Ministry of Health, 2017)

Hemodialysis procedure can accomplish frequent complications related to ESRD (Himmelfarb, 2005). Anemia is a frequent complication among ESRD patients that affects almost all patients undergoing HD (Strippoli and Clinical Evaluation of the, 2010, Jiang et al., 2013).

Anemia is one of the most common manifestations and visible characteristics of chronic kidney disease (CKD) contributing to mortality and morbidity (Al-Ali et al., 2015); adverse cardiovascular outcomes and poor health-related quality of life (HRQOL) (Strippoli and Clinical Evaluation of the, 2010).

Managing anemia in patients received renal replacement therapy is contentious despite the availability of erythropoietin stimulating agents

(ESAs) which are considered as a standard therapy for anemia in CKD patients (Ornt et al., 2013, Al-Ali et al., 2015).

On the other hand, HD can bring about significant impairment in HRQOL whether from the process of dialysis itself or its related comorbidity that affects patient`s social and psychological function (Zyoud et al., 2016). Furthermore, impaired HRQOL has been reported as a marker for poor outcomes in HD patients (Ibrahim and El Salamony, 2008, Mujais et al., 2009). In recent years, studies that intended to evaluate the treatment modalities and determined the mortality and morbidity in patients on HD; put greater interest in studying HRQOL among those patients (Lopes et al., 2002, Mapes et al., 2003).

Deterioration of HRQOL increased over time, one of its anticipated factor was the changes in hemoglobin (Hb) level (Soni et al., 2010). Moreover, previous studies have suggested a correlation between HD, anemia and diminished HRQOL (Soni et al., 2010, Sadeghi et al., 2016).

1.1.1 Anemia in CKD

Chronic kidney disease associated with serious complications that affects body homeostasis, one of the most common complications is anemia.

Anemia of renal failure was first observed by Richard Bright (later Sir Robert Christison) in 1839; he noted that *"by far the most remarkable character of the blood in the advanced stage of the Bright's disease is a gradual and rapid reduction of its coloring"* and *"no other natural disease*

came as close to hemorrhage for impoverishing the red particles of the blood." Similarly, Richard Bright had noticed that patients with kidney disease had paleness of the skin: *"after a time, the healthy color of the countenance fades*" (Cameron, 1999)

Anemia appears as early as stage 3 CKD (Alldredge et al., 2013); but relatively become more severe and frequent in more advanced stages of the disease (Fishbane and Spinowitz, 2018).

Although, anemia is well identified as a complication of CKD, the association between the grade of renal insufficiency and the decline in hematocrit is not effectively defined. A study at Boston health clinics published in 2001 concluded that there is an apparent decrease in hematocrit level in patient with creatinine clearance (CrCL) < 60 ml/min and men have larger decreased in hematocrit than women (Hsu et al., 2001).

The Third National Health and Nutrition Examination Survey (NHANES III) (1988 to 1994); analyzed hemoglobin, iron profile and serum creatinine in order to asses iron status, quantify the relationship between hemoglobin level and the rate of reduction in kidney function and estimate the likelihood of anemia in adults patients (>18 years) with different stages of CKD (Hsu et al., 2002). The results showed that the reduction in hemoglobin level is contributed with even a mild decrease in kidney function. In addition, men have larger decreased in hemoglobin level than women at any given level of CrCL; the apparent decrease in hemoglobin

level begin when CrCL ≤ 70 ml/min in men and ≤ 50ml/min in women. For example, compared with subjects with CrCl > 80 ml/min, the decrease in hemoglobin for subjects with CrCl 20 to 30 ml/min was 1.0 g/dl in women and 1.4 g/dl in men. Results also demonstrate that 46% of women and 19% of men had transferrin saturation (TSAT) < 20%; and 47% of women, 44% of men had serum transferrin < 100ng/ml when CrCL between 20-30 ml/min (Hsu et al., 2002).

On the other hand, the Kidney Early Evaluation Program (KEEP 2.0) from August 2000 to December 2001, measured serum creatinine in individuals with a high risk for developing kidney disease and patients with CKD and assessed the prevalence of anemia and diabetes at different stages of kidney function (El-Achkar et al., 2005). Results determined that 15.9%, 26.9% and 7.7% of the participants had diabetes, anemia and moderate decrease in kidney function (EGFR < 60ml/min/1.73m^2) respectively. In addition, the study concluded that there is an independent correlation between anemia and diabetes in patients with different level of EGFR (EGFR < 60ml/min/1.73m^2), and that the prevalence of anemia in men with diabetes is higher than that in women (El-Achkar et al., 2005).

The main reason for anemia in patients with CKD is a reduced in red blood cell (RBC) production; as erythropoiesis depend on sufficient accessibility of both erythropoietin and iron (Thomas et al., 2008, Alldredge et al., 2013, Fishbane and Spinowitz, 2018). Erythropoietin: which is a glycoprotein produced by an approximately 90% from renal cortical interstitial, its

deficiency in CKD is the key limit for reduced RBC production in bone marrow. In addition, iron deficiency in patients with CKD occurred in more than fifty percent of non-dialysis patients and in greater percentage in patients receiving HD, with an estimated loss of more than 2000 mg of iron per a year through HD (Fishbane and Spinowitz, 2018). Other factors contributed to anemia in CKD in addition to diminished RBC production are shortened erythrocyte survival, blood loss, hemolysis, inflammation, infection, nutritional deficits, folate and vitamin B12 deficiency and underlying hematologic disease (Thomas et al., 2008, Alldredge et al., 2013, Fishbane and Spinowitz, 2018).

1.1.2 Symptoms and complication related to anemia in CKD

Fatigue, shortness of breath, headache, reduced mental status and insomnia are nonspecific symptoms of anemia produced as a result of decrease oxygen supply to body tissues and organs (Thomas et al., 2008, Alldredge et al., 2013, Fishbane and Spinowitz, 2018).

Cardiovascular complication is a consequence as anemia progresses in CKD patients, including angina, left ventricular hypertrophy (LVH) and heart failure (Thomas et al., 2008, Alldredge et al., 2013). LVH was detected in 30% of patients with stage 2 and 3 CKD and 74% at stage 5 CKD (Alldredge et al., 2013).

1.1.3 Diagnosis and evaluation of anemia in CKD

The 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guideline defines anemia in children > 15 years and adults with CKD as Hb < 13.0 g/dl in males and < 12.0 g/dl in females (Appendix 1,Table 1.1), (KDIGO Board Members, 2012).

Hemoglobin testing should be performed periodically at all stages of CKD at different frequency manner based on the presence or absence of anemia, CKD stages, whether patient receiving ESA therapy or not and type of dialysis; HD or peritoneal dialysis (PD) (KDIGO Board Members, 2012).

KDIGO recommended measuring Hb level in non-anemic CKD patients at least annually in stage 3, every 6 months in stage 4 and non-dialytic stage 5 and every 3 months in dialytic stage 5. In addition, for anemic patients not receiving ESA, Hb level is recommended to be monitored at least every 3 months from stage 3 to non-dialytic and PD stage 5 and monthly in HD patients (KDIGO Board Members, 2012).

For initial evaluation of anemia, regardless the age and CKD stages, several blood tests are suggested to be performed including complete blood count (CBC), absolute reticulocyte count, iron indices, folate and vitamin B-12 serum level.

Complete blood count results, involving red cell indices, platelet count, white blood cell count and differential, Hb concentration, indicated the severity of anemia. Absolute reticulocyte is simply provide an information

about the readiness of bone marrow to response to anemia and the effectiveness of erythropoietic proliferative activity (Fishbane and Spinowitz, 2018).

On the other hand, macrocytic anemia resulted from folate or vitamin B-12 deficiencies, whereas microcytic anemia caused from iron deficiency.

Assessment of iron status is crucial for initiation of iron replacement and before starting treatment with ESA, as the deficiency in iron is a precipitating factor that lead to ESA hypo responsiveness and therefor sub optimized anemia (Van Wyck et al., 1989). TSAT and serum ferritin are the most widely used tests for assessing iron status. Ferritin is an iron binding protein play an important role in iron hemostasis and intracellular iron storage while serum ferritin is indirectly reflects the total body iron stores (Wang et al., 2010), in addition TSAT which is calculated by divided the serum iron by total iron binding capacity demonstrate the percentage of transferrin protein that carry iron and assess the availability of circulating iron (Worwood and May, 2006). KDIGO recommended measurement TSAT and serum ferritin at least every 3 months during ESA administration and in more frequent pattern if ESA therapy initiation or increasing dose is required, monitoring response to iron repletion therapy and in any condition associated with iron depletion (Cattran et al., 2012), (KDIGO Board Members, 2012).

KDIGO 2012 recommended to achieve Hb level in adult 10-11.5 g/dl, serum ferritin ≥ 500ng/ml and TSAT ≥30% (KDIGO Board Members, 2012).

1.1.4 Treatment of anemia in CKD

Several treatment approaches; blood transfusion, iron replacement and ESA therapy are clinically indicated for anemia management in CKD patients.

Adequate iron availability is the most important components required for the effectiveness of ESA therapy and prevent worsening of anemia (Fishbane and Maesaka, 1997, Fishbane et al., 1996, Van, 1989).

Administration of iron supplement is crucial in order to maintained its availability therefore treat its deficiency, prevent its declining with ESA therapy, increase Hb level in absence or presence of ESA and reduce the dose of ESA once indicated (KDIGO Board Members, 2012).

According to KDIGO recommendation, iron therapy should be administered after assessing the benefits of its administration and the risk for potential adverse effect. Generally, either oral or intravenous rout of iron can be considered. The decision for initiation or continuing iron supplementation in patients receiving ESA required regular evaluation for TSAT and serum ferritin at least every 3 months (KDIGO Board Members, 2012).

In addition, the standard therapy for anemia in CKD is ESA, and its administration has a beneficial outcome in reducing blood transfusion which is associated with blood borne viral disease transmission and prolonged or even the failure the chance of kidney transplantation (KDIGO Board Members, 2012).

Although ESA therapy is the mainstay treatment for anemia of CKD; its cost and poor response to ESA is considered as a challenge in the management of anemia. Several reasons influence the ESA hyporesponssivenes such as insufficient dialysis, blood loss, iron deficiency, hyperparathyrodism, inflammation, infection ,noncompliance and bone marrow disorder (Johnson et al., 2007, Zuo et al., 2016).

The 2012 KDIGO recommendations for use of iron supplementation and ESA in patients with CKD are represented in Appendix 1, (Table1.2,1.3,1.4).

1.2 Statement of problem

The most inclusive goal for the treatment of patients with ESRD is not only restricted on maintaining long survival rate, but also preserving patent's life at satisfactory level with improved quality of life (Seica et al., 2009).

Good anemia control had a positive impact on HD patients including lower mortality and morbidity risk with a substantial improvement of HRQOL (Pisoni et al., 2004, Singh et al., 2006, Akel et al., 2017).

Anemia management in ESRD is a challenge for health care providers as well as for the patients themselves (Akel et al., 2017), whereas inappropriate management is associated with poor outcomes and HRQOL. Few studies have been done to evaluate the anemia management among patients on HD and its correlation with HRQOL, and fortunately, none of these studies were conducted in Palestine.

This study may increase the knowledge about the disease and its management, aiding both the medical staff and the patients to improve their HRQOL. Moreover, this may help in decreasing therapeutic failure, the need for hospitalization and even death.

1.3 Research objectives

1.3.1 General objective

The main objective of the current study was to evaluate anemia management among patient on maintenance HD.

1.3.2 Specific objectives:

1. To assess HRQOL of patients on HD including anemic patients.

2. To determine the demographic, clinical characteristics of the study patients that were associated with anemia in HD patient.

3. To assess the association between anemia and HRQOL, demographic characteristics and disease related factors in HD patients.

1.4 Significance of the study

The previous studies aimed to define HRQOL association with HD (Zyoud et al., 2016), few studies have been established in order to study the management of anemia among patients on HD and it correlation to HRQOL (Soni et al., 2010, de Goeij et al., 2014). However**,** our study is the initial in Palestine focusing this issue. Therefore, this research gives a framework and information that evaluates anemia management, and data about anemia and its association with HRQOL, demographic and clinical characteristics of HD patients from Palestine.

In addition, determination of HRQOL and other factors associated with low Hb level among HD patients and evaluation of the treatment strategy can help in improving the treatment approach of those patients.

1.5 Literature Review

Anemia is a common feature of ESRD that is associated with poor outcomes including a reduction in HRQOL, increase the risk for hospitalization and death.

In recent years, a greater interest has been introduced to study the appropriateness of anemia management strategies and to investigate the relationship between anemia and HRQOL (Pisoni et al., 2004).

A study was performed in Saudi Arabia in 2008 aimed to review the management manner for anemia in HD patients and to check out its

appropriateness by comparing the noticed pattern to KDOQI guideline recommendation (Al-Ageel et al., 2012). This study was carried out over 7 months retrospectively and prospectively, the collected data included anemia status, iron administration, ESAs dosing besides patient's demographic and clinical characteristics.

Study enrolled 87 patients on maintaining HD with a mean age 50 ± 14 years, and the majority of patients received HD for ≥ 2 years. In addition, diabetic nephropathy was the precipitating reason of ESRD and hypertension is the most common complication. The study found that 45% of patients had mean Hb level between 11.0 and 12.0 g/dl which is within the target range recommended by KDOQI, 30% between 10.0-11.0 g/dl, 10% lower than 10.0g/dl and 15% above 12.0g/dl. In addition, the mean dose of erythropoietin per week was 135 ± 99 IU/kg/week, the study proved that a smaller dose of erythropoietin used with higher Hb level.

According to iron therapy and monitoring, only 81.6% of patients received iron replacement, 55.2% and 59.8% had recorded serum ferritin and TSAT value respectively. And 21.8% of patients were recorded for both ferritin and TSAT. The study also showed that females and patients with lower albumin level had a statistically significant lower Hb levels (Al-Ageel et al., 2012).

The European Survey of Anemia Management 2003 (ESAM 2003) (Jacobs et al., 2005a), has been conducted in 11 European countries (Austria, Belgium, Finland, Germany, Greece, The Netherlands, Poland, Slovenia,

Sweden, Switzerland and the UK) and Israel. It aimed to judge the managing of anemia in ESRD after the development of The European Best Practice Guidelines (EBPG) for handling with anemia in patients with ESRD at 1998 and evaluate whether the management of anemia had enhanced after four years of its introduction. Collected data included patient's demographic characteristic, clinical characteristic including cause of renal failure, concomitant disease and type of dialysis, laboratory data and epoetin therapy. Results revealed that diabetic nephropathy is the most verified reason of renal failure, hypertension is the communal comorbidity and the majority of precipitants had received HD. In addition, 66.1% of participants had Hb level ≥ 11 g/dl, 36.7% ≥ 12 g/dl, however, 13.2% had Hb level below 10 g/d. The percentage of patients accomplished to target Hb level (≥ 11 g/dl) varied among countries with highest proportion in Switzerland, Sweden and Belgium, more than 75% of their patients reached the target. While lower proportion in Greece and Poland, less than 65% of patients achieved it, however Germany, Netherlands and the UK failed to reached the stated target hemoglobin in more than 65% of their patients. For patients who had treated with epoetin for more than 3 months, 65.7% of them had a target hemoglobin concentration. Moreover, iron status was available for 91% of surveyed patients. Overall 90.75% and 63.83% of precipitant had available serum ferritin and TSAT respectively. 89.7% had a serum ferritin ≥100 ng/ml and 31% had TSAT < 20%. Only 48% of patients with epoetin therapy for more than 3 months had adequate iron status with serum ferritin ≥ 100 ng/ml and TSAT ≥20% as stated in EBPG.

Furthermore, in all countries the dose of epoetin was generally higher in patients not attained the goals of management compared with patients who achieved Hb level ≥ 11g/dl. In addition, the study concluded that there was an improvement in anemia management with EBPG, however many patients still have Hb level below the recommended. Thus, the study suggested that for better improvement there is a need for optimal iron supplementation and monitoring, adequate epoetin therapy and assessing the factors associated with its resistance (Jacobs et al., 2005b).

Gulf Survey on Anemia Management (GSAM) (Alsuwaida et al., 2007) is a retrospective survey of adult patients with ESRD undergoing chronic dialysis, in six Arabian Gulf countries including Saudi Arabia, Kuwait, Bahrain, Oman, United Arab Emirates and Qatar. The survey was done to confirm the fulfillment of the clinicians in the Arabian Gulf countries in the management of anemia according to the practical international guidelines. In GSAM, diabetic nephropathy was the leading factors for ESRD, and hypertension was the most prevalence comorbidity followed by type 2 diabetes, ischemic heart disease and viral hepatitis. The mean Hb level was 11.5 ± 1.5g/dl; 28% had Hb levels ≥ 11.0 g/dL, 38% had a Hb levels ≥ 12.0 g/dL, and 16% had Hb levels <10.0 g/dL. In addition, from all countries only Bahrain achieved the target Hb level (≥11.0 g/dL) in more than 75% of patients, while in the other countries less than 65% achieved it. Moreover, according to iron status, serum ferritin level was available in 97% of patients; it was found that serum ferritin was ≥ 100 ng/ml in 90.5% of these patients. And 31% of patients with available TSAT level had

TAST below 20%. Only 63.8% of patients who had administered epoetin therapy for ≥ 3 months were having sufficient iron status with serum ferritin levels of ≥ 100 ng/ml and TSAT value of ≥ 20%. Moreover, the mean dose of epoetin varied among countries; higher doses were reported in Kuwait and Qatar; in contrast, lower doses were reported in Oman, while there was no significant difference in Hb level in these countries.

A prospective, multicenter observational study that was conducted over 6 months between 2013 and 2014 in Lebanon at two dialysis centers in Beirut aimed to assess the adherence of anemia management to KDOQI guideline, evaluate the impact of iron status on Hb level and identify the relationship between Hb level and morbidity (Akel et al., 2017). The data enrolled from 189 HD patients, include patient's demographic and clinical information. The patients' mean age was 57.28 years, and 54.9% of patients were male, and the most common concomitant disease was hypertension. The study data demonstrated that the mean Hb level was 10.29 ± 1.44g/dl, 26% of patients had Hb level within the target range (11-11.9g/dl) as recommended by KDOQI. Furthermore, there was a significant difference between the recommended and prescribed dose of erythropoietin and iron replacement. In addition, erythropoietin weekly dose was 100 IU/Kg/week, which is approximately one third of the recommended starting dose by KDOQI (50-100 IU/kg three time weekly). Moreover, there is a significant difference with Hb level and different iron status (Akel et al., 2017).

A multicenter cross sectional and prospective study conducted in Iran (Nafar et al., 2017), investigated adult HD patients who received HD from January 2015 to December 2015. This study aimed to assess the status of anemia in HD patients, identify factor associated with erythropoietin responsiveness, assess the relationship between the dose of erythropoietin and response in Hb and identify the lowest dose of erythropoietin responsible for a gradual increase in Hb level toward target. The collected data included patient's demographic information, clinical characteristics; cause of ESRD, concomitant disease, years of dialysis, medication, type and dose of ESA and laboratory results. The results demonstrated that 62.3% of the enrolled patients were older than 55 years, 58.4% were men, 37% of patients were receiving dialysis for 12-36 months. The mean Hb level was 10.7 ± 1.4 g/dL, according to KDIGO guideline 54.5% the precipitant were within the target. In addition, 28.3% of recruited patients were anemic, 3% had Hb level < 8g/dl and 17.2% had Hb level > 12g/dl. Furthermore, 95.5% of patients received ESA therapy, with a mean weekly dose 8180 ± 5001 IU/week (adjusted to body weight 128.5 ± 82 IU/kg/week). The total weekly dose of ESA was 4000-10000 IU in 52% of patients and a higher dose > 10000 IU in 33%. In this study the participants were categorized into 4 groups based on their Hb level; < 8g/dl, 8-10 g/dl, 10-12 g/dl and > 12 g/dl, for assessing the association between ESA dose and Hb level. The highest dose of ESA was for patients with Hb < 8g/dl and the lowest dose for patients with Hb > 12 g/dl. In addition, the effective dose of ESA for patients with Hb level 8-10 g/dl was 10000-12000 IU /

week. Moreover, 59.6 % of participants had adequate iron status, 31.8% had TSAT < 20%, and 33.5% had serum ferritin < 200 ng/ml. The results also conclude that, there was an association between lower Hb level and several factors include: younger patients, being female, patients received inadequate dialysis, malnutrition, low albumin level and elevated CRP value.

Moreover, an observational retrospective cohort study conducted in Palestine over two months during 2014 at Hebron governmental hospital, aimed to determine the management strategies and its compliance to NKF-KDOQI and KDIGO guidelines for diabetes mellitus, hypertension, dyslipidemia, bone mineral disorder and anemia in HD patients. This study cited NKF-KDOQI 2006 and 2007 goals for anemia in HD with Hb 11-12 g/dl, serum ferritin >200 ng/ml and TSAT >20%, in addition KDIGO 2012 goals Hb 9 -11.5 g/dl, serum ferritin >500 ng/ml and TSAT > 30%. The total number of enrolled patients was 158, 60.1% were male, the mean age 49.6 ± 18 years. The highest proportion of patients was from village, had middle education level and were not working. 2 -18 medications with mean (±SD) 9.92 ± 2.94 were used by patients' sample, calcium carbonate was the most commonly prescribed followed by alfacalcidol then iron and folic acid. 69.9% of patients received iron supplementation and only 5.1% received ESA, the mean Hb level (± SD) was 8.84 ± 1.52 g/dl. Regarding to target; 8.9% and 43% achieved the Hb goals of NKF-KDOQI and KDIGO respectively. TSAT percentage were not available for all patients while serum ferritin level was obtained for 67.7%. 57.6% and 46.8% of

them had serum ferritin > 200 ng/ml and > 500 ng/ml as recommended by NKF-KDOQI and KDIGO respectively. Also, the study shows no significant association between control of anemia and patients sociodemographic and clinical factors (Al-Ramahi and Namourah, 2016).

On the other hand, a cross sectional study carried out in Iran (Sadeghi et al., 2016) aimed to determine the relationship between anemia, HRQOL and some laboratory indices in HD patients. The collected data involved patient's demographic information, HRQOL questionnaire for patients on HD and laboratory results for sodium, potassium, calcium, phosphorus, creatinine, albumin, bilirubin and fasting blood sugar. According to patient's demographic characteristic, from 99 investigated patients 61.6% were male, the mean age was 5.98 ± 10.98 year and 63 patients were on dialysis for longer than 2 years. Results demonstrated a mean Hb level 10.36 ± 0.95 g/dL and hematocrit 32.60 ± 3.25%. The study also exhibited a positive significant correlation between Hb and hematocrit level with HRQOL. The results also showed a significant correlation between Hb and hematocrit level with albumin, bilirubin, potassium, calcium and phosphorous; while no significant correlation was found with glucose, creatinine and sodium. Furthermore, the use of erythropoietin resulted in an increased Hb level and subsequently an improvement in HRQOL.

Chapter Two
Methodology

2.1 Study design and setting

This study is a cross sectional observational study, achieved by using a convenience clustered sampling technique to address the research goals including the evaluation of anemia management in HD patients, assess HRQOL in these patients, to determine their demographic and clinical characteristics and assess the association between anemia and HRQOL, demographic characteristics and disease related factors in HD patients.

The sample was recruited from three dialysis centers from West Bank - Palestine; An-Najah National University Hospital – Nablus, Ramallah's Sons Ward in Palestine Medical Complex – Ramallah and Al Hussein Government Hospital - Beit Jala.

2.2 Sample size

The total number of patients who underwent dialysis at An-Najah National University Hospital, Ramallah's Sons Ward and Al Hussein Government Hospital by 2016 as reported in health annual report Palestine 2016 was 484 patients (Palestinian Ministry of Health, 2017). This number was used in calculating the sample size required for this study, using Roasoft sample size calculator (http://www.raosoft.com/samplesize.html), by means of response distribution 50% and 95% confidence interval margin of error 5%, the calculated minimum effective sample size was 216.

An-Najah National University Hospital received 48.97% of this sample, Ramallah's Sons Ward received 32.44%, and Al Hussein Government Hospital received 18.59% of this population. Thus, the 216 patients were distributed as the following: 106 patients from An-Najah National University Hospital, 70 patients from Ramallah's Sons Ward and 40 patients from Al Hussein Government Hospital. Moreover, the estimated sample size was increased by 5% - 10% in order to maximize the reliability of the current study and decrease false results. Furthermore, a pilot study of 10 - 20 patients was done before beginning the actual study.

2.3 Data collection

Data were collected from the three dialysis centers during the period from 24 June to 5 September 2018. The data were filled throughout the working time of each center by interviewing the enrolled patients for almost 10 min and then accessed their profiles.

2.3.1 Tools used in data collection

A data collection form (Appendix 2) consists of two parts.

The first part contains the patient’s demographic and clinical information divided as the following:

A. Socio-demographic characteristics including: age, gender, weight, height, level of education (illiterate, primary, secondary, university, postgraduate), family monthly income (low (less than 2000 NIS), moderate

(2000-5000 NIS), high (more than 5000 NIS)), marital status (married, single, divorced, widowed), locality (urban, rural, camp), employment status (unemployed, employed, previously employed before the failure onset), and family history of renal failure.

B. Clinical information about disease history and co-morbidities which include: number of dialysis per week, years of suffering from renal failure, years of undergoing HD, the interval of dialysis session, smoking (current smoker, previous smoker, nonsmoker, years of smoking), exercise, using herbal remedies, and the presence of co-morbidities (such as hypertension, DM, ischemic heart diseases).

C. Patient's current medications and last laboratory value.

The second part consists of the European Quality of Life 5- Dimensions scale (EQ-5D). The Euro QOL Group developed the EQ-5 D instrument, which consists of the descriptive system and the EQ visual analogue scale (EQ-VAS). The descriptive system comprises five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression). In addition, EQ-VAS records the respondent's self-rated health on a 20 cm vertical visual analogue scale with endpoints labeled 'the best health you can imagine' and 'the worst health you can imagine'. The EQ-VAS records how good or bad patient's health status is today by mark X on the scale and then write number on the box below. The Arabic version of EQ-5D was provided by using Euro QoL guidelines (Euroqol Group, 2013).

2.4 Inclusion and exclusion criteria

2.4.1 Inclusion criteria

1. ESRD patients on maintenance HD.

2. Patients aged 18 years and above.

3. Patients who agreed to participate.

2.4.2 Exclusion criteria:

1. Patients unable to understand the question, such as psychiatric patients.

2. Patients have cancer or are receiving chemotherapy.

2.5 Statistical analysis

Through the Statistical Package for Social Sciences (SPSS; SPSS Inc., Chicago, IL, USA) program version 16 the overall data were entered and analyzed. The continuous variable was presented as mean and standard deviation, while categorical variable as frequency and percentage and variable that was not normally distributed was expressed as median (lower-upper quartile). The Kolmogorov-Smirnov test was used for testing the normality of variables. The Mann-Whitney U test (a nonparametric equivalent of the t test) / Kruskal–Wallis was performed as appropriate when the assumptions of equality of variance and normality (assumed for the t test) were not seen. Either the Chi-square or the Fisher exact test, as appropriate, was used to test significance between categorical variables.

The Spearman correlation coefficient was used for assessing correlation. The level of significance determined when $p < 0.05$.

TSAT percentage that was not readily recorded was calculated for patients who had the available variables for its calculation; total serum iron, total iron binding capacity and serum transferrin.

For analyzing the association between Hb and HRQOL, demographic characteristics and disease related factors; an average Hb level 11g/dl used as a cut of point for Hb goal.

Additionally, the EQ-5D-5L Crosswalk Index Value Calculator, depending on values taken from the United Kingdom general population, was used for calculating the scores of EQ-5D.

2.6 Ethical Considerations

Permission from the Institutional review Board (IRB), Palestinian Ministry of Health, and An-Najah National University Hospital (Appendices 2, 3, 4) were obtained before initiation the research. In addition, a verbal consent form was gained from patient individually and only patients who accepted to participate were included in the study.

Chapter Three
Results

3.1 Demographic characteristics of the study sample

A total number of 226 patients on HD included in this study. The data collected from three dialysis centers in West Bank, Palestine. The distribution of those patients was as follow: 108 (47.8%) patients were from An-Najah National University Hospital - Nablus, 74 (32.7%) were from Ramallah's Sons Ward in Palestine Medical Complex - Ramallah and 44 (19.5%) were from Al Hussein Government Hospital - Beit Jala.

Table 3.1 shows the demographic characteristics of the patients. The mean age (± SD) of patients was 57 ± 13.9 years, ranging from 21 to 87 years. More than half of patients (n=121, 53.5%) were male. The largest portion (n=117, 51.8%) of patients were living in rural, followed by (n=86, 38.1%) urban areas. The marital status reported by patients was as the following: 78.8% were married and 21.2% were single/ divorced/ widowed. About the education level; the majority (n=86, 38.1%) of patients had secondary education, followed by (n=80, 35.4%) a primary education. A small proportion (n=13, 5.8%) of patients reported that they have current job, while 124 (54.9%) were previously employed.

Furthermore, the mean weight (± SD) of patients was 75.65 ± 17.03 kg, ranging from 37 to 149 kg. The majority (n=136, 60.2%) of patients were non-smoker. Only 7.5% of patients did exercise.

On the other hand, out of 226 participants; 39 (17.3%) patients reported that they have family history of renal disease.

Table 3.1 Demographic characteristics of the study sample

Characteristic	**Total (n=226)**
Dialysis center, n (%) An-Najah National University Hospital – Nablus Al Hussein Ramallah's Sons Ward in Palestine Medical Complex – Ramallah Government Hospital - Beit Jala	 108 (47.8) 74 (32.7) 44 (19.5)
Gender, n (%) Male Female	121 (53.5) 105 (46.5)
Age (years) Mean ± SD Range	 57 ± 13.9 21-87
Age category (years) < 30 30-60 > 60	 13 (5.8) 111 (49.1) 102 (45.1)
Locality, n (%) Rural Urban Camp	 117 (51.8) 86 (38.1) 23 (10.2)
Marital status, n (%) Married Single Divorced Widowed	 178 (78.8) 27 (11.9) 2 (0.9) 19 (8.4)
Level of education, n (%) Illiterate Primary Secondary University Postgraduate	 19 (8.4) 80 (35.4) 86 (38.1) 38 (16.8) 3 (1.3)
Employment status, n (%) Unemployed Employed Previously employed before renal failure	 89 (39.4) 13 (5.8) 124 (54.9)
Income of family, n (%) Low (less than 200 NIS)	 6 (2.7)
Weight (kg) Mean ± SD Range	n=225 75.65 ± 17.03 37-149
Smoking, n (%) Current smoker Previous smoker Non-smoker	 52 (23) 38 (16.8) 136 (60.2)
Exercise, n (%)	

Characteristic	Total (n=226)
No yes	209 (92.5) 17 (7.5)
Family history, n (%) No Yes	 187 (82.7) 39 (17.3)

Abbreviations: NIS: new Israeli shekel, SD: standard deviation.

3.2 History of renal disease of the study sample

As shown in Table 3.2, the median (interquartile range) of years that the patients had been suffering from renal failure and the years in which those patients undergoing HD was 4.0 (2.0 - 6.0) and 2.5 (1.0 - 5.0), respectively. In addition, the median number (interquartile range) of dialysis per week was 3.0 (3.0 - 3.0), with median of hours (interquartile range) of dialysis session was 3.5 (3.5 - 4).

Table 3.2 History of renal disease of the study sample

Variable	Median (Interquartile range)
Number of dialysis session per week	3 (3 - 3)
Years of renal failure	4 (2 - 6)
Years of dialysis	2.5 (1 - 5)
Hours of dialysis	3.5 (3.5 - 4)

3.3 Herbal remedies used by the study sample

The results show that 123 patients (54.4%) used herbal remedies; Arabic Gum (n=71,31%) was the most popular herbs used, followed by mixed herbs (n=42,18.6%)

Table 3.3 Herbal remedies used by the study sample

Herbs	**Total (n = 226) n (%)**
Arabi gum	71 (31.4)
Mixed herbs	42 (18.6)
Parsley	18 (8)
Anise	16 (7.1)
Chamomile	11 (4.9)
Honey	11 (4.9)
Fenugreek	10 (4.4)
Barely	10 (4.4)
Rosemary	7 (3.1)
Vervain	4 (1.8)
Nigella	3 (1.3)
Sage	3 (1.3)
Frankincense	2 (0.9)
Ginger	2 (0.9)
Fennel	1 (0.4)
Peppermint	1 (0.4)
Tilia	1 (0.4)
Thyme	1 (0.4)
Radish	1 (0.4)
Saffron	1 (0.4)
Urtica	1 (0.4)
Kefir	1 (0.4)
Anabasis	1 (0.4)
Teucrium	1 (0.4)

3.4 Comorbid diseases among the study sample

The majority of patients suffered from hypertension (n=198, 87.6%), followed DM (n=127, 56.2%), (Table 3.4).

Regarding to the presence of comorbid disease the median (interquartile range) of total number of comorbid diseases among patients was 4 (3-5.12). In addition, 0.4% of patients had no comorbid disease, 2.2% had only one comorbid disease, 11.5% had two comorbid diseases, 17.7% had three comorbid diseases and 68.1% had four and more comorbidities, (Table 3.5).

Table 3.4 Comorbid diseases among the study sample

Co-morbid disease	**Total (n = 226) n (%)**
Hypertensions	198 (87.6)
Diabet1es Mellitus	127 (56.2)
Ischemic heart disease	96 (42.5)
Heart failure	61 (27)
Hyperparathyroidism	48 (21.2)
Dyslipidemia	40 (17.7)
Gout	38 (16.8)
Retinopathy	26 (11.5)
Osteoarthritis	21 (9.3)
Nephrotoxicity	20 (8.8)
Urinary tract infection	19 (8.4)
Urinary stones	15 (6.6)
Hypothyroidism	12 (5.3)
Polycystic kidney disease	10 (4.4)
Atrophic kidney	9 (4)

Co-morbid disease	**Total (n = 226) n (%)**
Atrial fibrillation	7 (3.1)
Benign Prostatic Hypertrophy (BPH)	6 (2.7)
Asthma	5 (2.2)
Gastroesophageal Reflux Disease (GERD)	4 (1.8)
Osteoporosis	4 (1.8)
Chronic Obstructive Pulmonary Disease (COPD)	3 (1.3)
Hepatitis	3 (1.3)
Glaucoma	3 (1.3)
Familial Mediterranean Fever (FMF)	2 (0.9)
Meniere's syndrome	2 (0.9)
Systemic infection	1 (0.4)
Rheumatoid arthritis	1 (0.4)
Systemic Lupus Erythematosus (SLE)	1 (0.4)
Glomerular Nephritis	1 (0.4)
Crohn's disease	1 (0.4)
Psoriasis	1 (0.4)
Alport syndrome	1 (0.4)
Hypoparathyroidism	1 (0.4)

Table 3.5 Total diseases among the study sample

Number of comorbid diseases	**Total (n = 226) n (%)**
No comorbid disease	1 (0.4)
One comorbid disease	5 (2.2)
Two comorbid diseases	26 (11.5)
Three comorbid diseases	40 (17.7)
Four and more comorbid diseases	154 (68.1)

3.5 Chronic medications used by the study sample

Regarding medications used, the range number of medications used among patients was 0-14, with a mean (±SD) of 6.53 ± 2.37 and a median (interquartile range) of 6 (5-8).

As shown in Table 3.6, according to patient's medications; Darbepoetin (n=196, 86.7%) Calcium carbonate (n=193,85.4%), Alfacalcidol (n=190,84.1%) and Iron III- hydroxide sucrose (n=128, 56.64%) were the most commonly used medications.

Table 3.6 Chronic medications used by the study sample

Medication	**Total (n = 226) n (%)**
Darbepoetin Dose (mcg): mean ± SD 30 mcg 60mcg 90mcg	196, (86.7) 42.1 ± 16.2 122 (62.2) 69 (35.2) 5 (2.6)
Calcium carbonate	193 (85.4)
Alfacalcidol	190 (84.1)
Iron III- hydroxide sucrose (IV) Dose (mg)	128 (56.64) 100
Aspirin	102 (45.1)
Amlodipine	80 (35.4)
Ranitidine	75 (33.2)
Insulin	66 (29.2)
Atorvastatin	66 (29.2)
Furosemide	64 (28.3)
Sevelamer	55 (24.3)
Paracetamol	42 (18.6)
Bisoprolol	41 (18.1)

Medication	**Total (n = 226) n (%)**
Allopurinol	29 (12.8)
Clopidogrel	26 (11.5)
Isosorbide mononitrate	23 (10.2)
Omega 3	18 (8)
Enalapril	17 (7.5)
Enoxaparin	16 (7.1)
Carvedilol	13 (5.8)
Doxazosin	12 (5.3)
Atenolol	11 (4.9)
L- Thyroxin	11 (4.9)
Esomeprazole	9 (4)
Folic acid	9 (4)
Nifedipine	8 (3.5)
Warfarin	8 (3.5)
Loratadine	8 (3.5)
Prednisolone	4 (1.8), Total (n= 225)
Valsartan	4 (1.8)
Hydralazine	4 (1.8)
Omeprazole	4 (1.8)
Colchicine	4 (1.8)
Amlodipine / Valsartan	3 (1.3)
Glimepiride	3 (1.3)
Ipratropium Bromide	3 (1.3)
Betahistine	3 (1.3)
Cinacalcet	3 (1.3)
Sodium valproate	3 (1.3)
Phenytoin	3 (1.3)
Labetalol	2 (0.9)
Amiodarone	2 (0.9)
L-Dopa	2 (0.9)

Medication	**Total (n = 226) n (%)**
Midodrine	2 (0.9)
Vildagliptin	2 (0.9)
Tamsulin	2 (0.9)
Carbamazepine	1 (0.4), Total (n= 225)
Lercanidipine	1 (0.4)
Sacubitril / Valsartan	1 (0.4)
Metolazone	1 (0.4)
Metformin	1 (0.4)
Saxagliptin	1 (0.4)
Glibenclamide	1 (0.4)
Pantoprazole	1 (0.4)
Vitamin B-12	1 (0.4)
Chlorpheniramine	1 (0.4)
Montelukast	1 (0.4)
Alfuzosin	1 (0.4)
Bezafibrate	1 (0.4)
Bisacodyl	1 (0.4)
Gabapentin	1 (0.4)
Pregabalin	1 (0.4)
Clonazepam	1 (0.4)

Abbreviation: IV: intravenous, SD: standard deviation

3.6 Hemoglobin level for the study sample

As shown in Table 3.7, the mean Hb level (± SD) was 10.63 ± 1.71g/dl ranging from 6.10 to 17.31g/dl.

According to anemia definition by KDIGO, 109 (90.1%) of male patients were anemic with Hb < 13g/dl and 83 (79%) of female patients were anemic with Hb < 12g/dl.

With reference to KDIGO recommendation for Hb level, 84 (37.16%) patients had Hb value < 10g/dl, 134 (59.3%) patients had Hb value < 11g/dl, 92 (40.7%) had Hb value > 11g/dl and 77 (34.1%) had Hb value 10-11.5g/dl which is within target level.

Table 3.7 Hemoglobin level of the study **sample**

Hb level (g/dl)	**Total (n=226)n (%)**
Mean ± SD Range	10.63 ± 1.71 6.10 – 17.31
Male Hb < 13 Hb > 13	n= 121 109 (90.1) 12 (9.9)
Female Hb < 12 Hb > 12	n= 105 83 (79) 22 (21%)
Hb < 11	134 (59.3)
Hb > 11	92 (40.7)
Hb 10-11.5	77 (34.1)
Hb < 10	84 (37.16)

Abbreviation: Hb: Hemoglobin, SD: Standard deviation

3.7 Iron status monitored for the study sample

As shown in table 3.6; out of 226 patients, 128 (56.6%) patients received iron replacement therapy via intravenous rout. All 128 patients used iron III -hydroxide sucrose with dose 100 mg.

Information about iron status was available as the following; 163 (72.1%) patients had recorded serum ferritin and 185 (81.90%) had recorded TSAT (Table 3.8).

The mean (±SD) TSAT of patients was 32.33 ± 17.16% ranging from 5.41 to 130, the mean (±SD) serum ferritin was 447.49 ± 464.45 ng/ml ranging from 4.63 to 2016.

Relating to KDIGO goals, from 163 patients recorded for serum ferritin; 54 (33.1%) patients had serum ferritin ≥ 500 ng/ml. And from 185 patients recorded for TSAT 93 (50.3%) patients had TSAT ≥ 30%.

Table 3.8 Iron status recorded for the study sample

Lab test	**Total (n=226)**
Serum ferritin (ng/ml)	
n (%)	163 (72.1)
Mean ± SD	447.49 ± 464.45
Range	4.63 – 2016
< 500	109 (66.9)
≥ 500	54 (33.1)
TSAT (%)	
n (%)	185 (81.9)
Mean ± SD	32.33 ± 17.16
Range	5.41 – 130
< 30	92 (49.7)
≥ 30	93 (50.3)

Abbreviation: TSAT: Transferrin saturation, SD: Standard deviation

3.8 Erythropoietin stimulating agent used in the study sample

The results show that 196 (86.7%) patients used Darbepoetin, the mean (± SD) administered dose was 42.1 ± 16.2 mcg. Among 196 patients; 122 (62.6%) patients received 30 mcg, 69 (35.2%) received 60 mcg and 5 (2,6%) received 90mcg (Table 3.6).

Regarding to initiation of ESA; from the 30 patients (13.3%) who didn't receive ESA; 20% (n=6) had Hb level > 13g/dl as suggested by KDIGO not required to initiate of ESA.

However, from 37.2% (n=84) of patients had Hb level < 10g/dl (Table 3.7), 2.4% (n=2) were not initiated with ESA therapy unless its recommendation according to KDIGO (Table 3.9).

Regarding to maintaining use of Darbepoetin according to KDIGO, from the 196 patients who received it 24% (n=47) had Hb level > 11.5 g/dl which suggest not to maintain ESA use (Table 3.9).

Table 3.9 Hemoglobin level and Darbepoetin administration in the study sample

Hb level (g/dl)	**Total (n=226)**
Received Darbepoetin Hb > 11.5 Hb ≤ 11.5	196 (86.7) 47(24) 149 (76)
Not received Darbepoetin Hb > 13 Hb <10	30 (13.3) 6 (20) 2 (2.4)

Abbreviation: Hb:Hemoglobin

3.9 Some laboratory indices recorded for the study sample

Table 3.10 shows a variety of laboratory results obtained for patients including c-reactive protein, albumin, total bilirubin, blood urea nitrogen,

fasting blood glucose, serum creatinine, phosphorous, calcium, potassium and sodium.

Table 3.10 Some laboratory indices recorded for the study sample

Lab test	**Total (n=226)**
C- reactive protein (mg/l) n (%) Mean ± SD Range	 29 (12.8) 22.22 ± 50.49 0.49 – 272
Albumin (g/dl) n (%) Mean ± SD Range	 182 (80.5) 3.82 ± 0.48 1 – 5.62
Total bilirubin (mg/dl) n (%) Mean ± SD Range	 36 (15.9) 0.37 ± 0.15 0.2 – 0.8
Blood urea nitrogen (mg/dl) n (%) Mean ± SD Range	 222 (98.2) 55.73 ± 54.85 4.30 – 728
Fasting blood glucose (mg/dl) n (%) Mean ± SD Range	 109 (48.2) 140.69 ± 86.37 63 – 683
Serum creatinine (mg/dl) n (%) Mean ± SD Range	 223 (98.7) 7.89 ± 3.08 0.92 – 21.3
Phosphorus level (mg/dl) n (%) Mean ± SD Range	 225 (99.6) 10.71 ± 43.93 0.94 – 441
Calcium level (mg/dl) n (%) Mean ± SD Range	 225 (99.6) 9.71 ± 8.12 6.14 – 95
Potassium level (mmol/l) n (%) Mean ± SD Range	 224 (99.1) 4.71 ± 0.90 2.70 – 7.40
Sodium level (mEq/l) n (%) Mean ± SD Range	 224 (99.1) 136.24 ± 13.07 3.92 – 154

Abbreviation: SD: Standard deviation

3.10 Socio-demographic characteristics of the study sample with differences in hemoglobin goal

Table 3.11 show patient's demographic characteristics and its association with hemoglobin goal; there is no significant association between Hb goal and age category, gender, locality, level of education, marital status, employment status, being smoker, doing exercise and family history of renal disease with p-value > 0.05.

Table 3.11 Demographic characteristics of patient sample vs hemoglobin goal

	n (%)			
Sociodemographic characteristics	**Total**	**Hb < 11g/dl**	**Hb ≥ 11g/dl**	**P-value**
Age category (years) < 30 30-60 >60	 13 (5.8) 111 (49.1) 102 (45.1)	 7 (5.2) 71 (53) 56 (41.8)	 6 (6.5) 40 (43.5) 46 (50)	0.334
Gender Male Female	 121 (53.5) 105 (46.5)	 66 (49.3) 68 (50.7)	 55 (59.8) 37 (40.2)	0.119
Locality Urban Rural Camp	 86 (38.1) 117 (51.8) 23 (10.2)	 53 (39.6) 65 (48.5) 16 (11.9)	 33 (53.9) 52 (56.5) 7 (7.6)	0.391
Level of education Illiterate Primary Secondary University Postgraduate	 19 (8.4) 80 (35.4) 86 (38.1) 38 (16.8) 3 (1.3)	 12 (9) 47 (35.1) 52 (38.8) 23 (17.2) 0 (0)	 7 (7.6) 33 (35.9) 34 (37) 15 (16.3) 3 (3.3)	0.334
Marital status Married Single Divorced Widowed	 178 (78.8) 27 (11.9) 2 (0.9) 19 (8.4)	 104 (77.6) 15 (11.2) 1 (0.7) 14 (10.4)	 74 (80.4) 12 (13) 1 (1.1) 5 (5.4)	0.591
Employment status Unemployed Employed Previously employed before	 89 (39.4) 13 (5.8) 124 (54.9)	 55 (41) 9 (6.7) 70 (52.2)	 34 (37) 4 (4.3) 54 (58.7)	0.555

	n (%)			
Sociodemographic characteristics	**Total**	**Hb < 11g/dl**	**Hb ≥ 11g/dl**	**P-value**
renal failure				
Smoking				0.227
Current smoker	52 (23)	33 (24.6)	19 (20.7)	
Previous smoker	38 (16.8)	18 (13.4)	20 (21.7)	
Non-smoker	135 (59.7)	83 (61.9)	52 (56.5)	
Exercise				0.508
No	209 (92.5)	122 (91)	87 (94.6)	
Yes	16 (7.1)	11 (8.2)	5 (5.4)	
Family history				0.501
No	187 (82.7)	109 (81.3)	78 (84.8)	
Yes	39 (17.3)	25 (18.7)	14 (15.2)	

Abbreviation: IQR: Interquartile range, p-value: probability value, Hb: hemoglobin.

3.11 Disease related factors of the study sample with differences in hemoglobin goal

As shown in table 3.12 there is no significant association between Hb target and number of dialysis per week, years of renal failure, total number of comorbid disease and chronic medications with p-value > 0.05.

However, there is a significant association (p-value = 0.031) between hemoglobin target and number of years the patients undergo hemodialysis.

Table 3.12 Disease related factors associated vs hemoglobin goal

	n (%) Median (IQR)			
Disease related factors	**Total**	**Hb < 11g/dl**	**Hb ≥ 11g/dl**	**P-value**
Number of dialysis				0.399
1	1 (0.4)	0 (0)	1 (1.1)	
2	24 (10.6)	15 (11.2)	9 (9.8)	
3	199 (88.1)	117 (87.3)	82 (89.1)	
4	2 (0.9)	2 (1.5)	0 (0)	
Years of renal failure		4 (1.6525-6)	4 (2-6.75)	0.331
Years of dialysis		2 (1-5)	3 (1.3125-5)	0.031
Total disease cut off				0.190
No comorbid disease	1 (0.4)	0 (0)	1 (1.1)	
One comorbid disease	5 (2.2)	1 (0.7)	4 (4.3)	
Two comorbid disease	26 (11.5)	13 (9.7)	13 (14.1)	
Three comorbid disease	40 (17.7)	25 (18.7)	15 (16.3)	
Four and more comorbid disease	154 (68.1)	95 (70.9)	59 (64.1)	
Total number of medications				0.174
	1 (0.4)	1 (0.7)	0 (0)	
No medication	1 (0.4)	1 (0.7)	0 (0)	
One medication	4 (1.8)	1 (0.7)	3 (3.3)	

	n (%) Median (IQR)			
Disease related factors	**Total**	**Hb < 11g/dl**	**Hb ≥ 11g/dl**	**P-value**
Two medications	14 (6.2)	5 (3.7)	9 (9.8)	
Three medications	29 (12.8)	20 (14.9)	9 (9.8)	
Four medications	177 (78.3)	106 (79.1)	71 (77.2)	
Five and more medications				

Abbreviation: IQR: Interquartile range, p-value: probability value, Hb: hemoglobin.

3.12 Health related quality of life of the study sample

This study measured HRQOL among participants. Table 3.13 shows the dimensions that used to measure HRQOL that include: Mobility, Self-care, Usual activity, Pain/discomfort, and Anxiety. The majority of patients (n=66, 29.2%) had moderate problems in waking followed by 22.6% (n=51) with no problem in waking. The largest portion (n=124, 54.9%) had no problem regarding their self-care. According to patient's regular activity, 32.3% (n=73) and 23.9% (n=54) had no and slight problems doing their usual activities, respectively. Most of patients (n=74, 32.7%) experienced moderate pain or discomfort. About patients feeling of anxiety or depression; 27.4% (n=62), 26.5% (n=60) and 25.2% (n=57) were moderately, slightly and non-anxious or depressed respectively.

Table 3.13 The dimensions that used to measure HRQOL among the study sample

Variable	**Total (n = 226) n (%)**
Mobility	
I have no problems in walking	51 (22.6)
I have slight problems in walking	45 (19.9)
I have moderate problems in walking	66 (29.2)
I have severe problems in walking	44 (19.5)
I am unable to walk	20 (8.8)
Self-care	
I have no problems washing or dressing myself	124 (54.9)
I have slight problems washing or dressing myself	29 (12.8)
I have moderate problems washing or dressing myself	29 (12.8)
I have severe problems washing or dressing myself	29 (12.8)
I am unable to wash or dress myself	15 (6.6)
Usual activity (e.g. work, study, housework, family or leisure activities)	
I have no problems doing my usual activities	73 (32.3)
I have slight problems doing my usual activities	54 (23.9)
I have moderate problems doing my usual activities	37 (16.4)
I have severe problems doing my usual activities	41 (18.1)
I am unable to do my usual activities	21 (9.3)
Pain/Discomfort	
I have no pain or discomfort	67 (29.6)
I have slight pain or discomfort	41 (18.1)
I have moderate pain or discomfort	74 (32.7)
I have severe pain or discomfort	25 (11.1)
I have extreme pain or discomfort	19 (8.4)
Anxiety/Depression	
I am not anxious or depressed	57 (25.2)
I am slightly anxious or depressed	60 (26.5)
I am moderately anxious or depressed	62 (27.4)
I am severely anxious or depressed	33 (14.6)
I am extremely anxious or depressed	14 (6.2)

3.13 Self-reported EQ-5D-5L health states and EQ-VAS

Table 3.14 describes the reported health states of patients, 162 states were reported, 12 patients (5.3%) reported no difficulty in any of the five dimensions, while 2 patients (0.9%) reported the highest degree of difficulty in the five dimensions.

The median (interquartile range) of EQ-5D-5L index was 0.69 (0.49-0.81) and for EQ-VAS score was 60 (50-75).

Table 3.14 Self-reported EQ-5D-5L health states

No.	EQ-5D Profile	Total (n = 226) n (%)	No.	EQ-5D Profile	Total (n = 226) n (%)	No.	EQ-5D Profile	Total (n = 226) n (%)
1	11111	12 (5.3)	55	24553	1 (0.4)	109	41111	1 (0.4)
2	11112	5 (2.2)	56	31111	1 (0.4)	110	41112	1 (0.4)
3	11113	1 (0.4)	57	31112	2 (0.9)	111	41133	1 (0.4)
4	11114	2 (0.9)	58	31113	1 (0.4)	112	41211	1 (0.4)
5	11121	2 (0.9)	59	31122	2 (0.9)	113	41214	1 (0.4)
6	11122	3 (1.3)	60	31123	1 (0.4)	114	41312	1 (0.4)
7	11123	2 (0.9)	61	31131	3 (1.3)	115	41343	1 (0.4)
8	11124	1 (0.4)	62	31133	1 (0.4)	116	41355	1 (0.4)
9	11131	3 (1.3)	63	31141	1 (0.4)	117	41434	2 (0.9)
10	11211	1 (0.4)	64	31143	1 (0.4)	118	41454	1 (0.4)
11	11213	1 (0.4)	65	31152	1 (0.4)	119	41512	1 (0.4)
12	11221	1 (0.4)	66	31211	1 (0.4)	120	42134	1 (0.4)
13	11222	2 (0.9)	67	31212	1 (0.4)	121	42242	1 (0.4)
14	11233	1 (0.4)	68	31222	1 (0.4)	122	42243	1 (0.4)
15	11234	1 (0.4)	69	31223	1 (0.4)	123	42311	1 (0.4)
16	11243	1 (0.4)	70	31231	1 (0.4)	124	42332	1 (0.4)
17	11311	1 (0.4)	71	31232	2 (0.9)	125	42423	1 (0.4)
18	11314	1 (0.4)	72	31233	2 (0.9)	126	42531	1 (0.4)
19	11322	2 (0.9)	73	31234	1 (0.4)	127	43232	1 (0.4)
20	11342	1 (0.4)	74	31244	1 (0.4)	128	43333	1 (0.4)
21	12222	2 (0.9)	75	31313	1 (0.4)	129	43343	1 (0.4)
22	12233	1 (0.4)	76	31325	1 (0.4)	130	43354	1 (0.4)
23	12332	1 (0.4)	77	31332	1 (0.4)	131	43431	1 (0.4)
24	13153	1 (0.4)	78	31334	1 (0.4)	132	43433	2 (0.9)
25	13333	1 (0.4)	79	31431	1 (0.4)	133	43521	1 (0.4)
26	15555	1 (0.4)	80	32211	1 (0.4)	134	43532	1 (0.4)
27	21111	4 (1.8)	81	32223	1 (0.4)	135	43544	1 (0.4)
28	21112	2 (0.9)	82	32232	1 (0.4)	136	44213	1 (0.4)

No.	EQ-5D Profile	Total (n = 226) n (%)	No.	EQ-5D Profile	Total (n = 226) n (%)	No.	EQ-5D Profile	Total (n = 226) n (%)
29	21113	1 (0.4)	83	32233	2 (0.9)	137	44231	1 (0.4)
30	21121	1 (0.4)	84	32322	2 (0.9)	138	44412	1 (0.4)
31	21122	5 (2.2)	85	32331	1 (0.4)	139	44413	2 (0.9)
32	21123	1 (0.4)	86	32334	1 (0.4)	140	44443	1 (0.4)
33	21124	1 (0.4)	87	32335	1 (0.4)	141	44444	4 (1.8)
34	21125	1 (0.4)	88	32353	1 (0.4)	142	44445	1 (0.4)
35	21131	1 (0.4)	89	32414	1 (0.4)	143	44554	1 (0.4)
36	21132	2 (0.9)	90	32433	1 (0.4)	144	45413	1 (0.4)
37	21133	1 (0.4)	91	33133	1 (0.4)	145	45525	1 (0.4)
38	21145	1 (0.4)	92	33231	1 (0.4)	146	45543	1 (0.4)
39	21211	5 (2.2)	93	33241	1 (0.4)	147	51135	1 (0.4)
40	21222	1 (0.4)	94	33311	1 (0.4)	148	51452	1 (0.4)
41	21224	1 (0.4)	95	33314	1 (0.4)	149	53313	1 (0.4)
42	21231	1 (0.4)	96	33323	1 (0.4)	150	53414	1 (0.4)
43	21232	2 (0.9)	97	33331	2 (0.9)	151	54412	1 (0.4)
44	21233	3 (1.3)	98	33333	2 (0.9)	152	54432	1 (0.4)
45	21331	1 (0.4)	99	33432	1 (0.4)	153	54433	2 (0.9)
46	21412	1 (0.4)	100	33432	1 (0.4)	154	54434	1 (0.4)
47	22213	1 (0.4)	101	33441	1 (0.4)	155	55452	1 (0.4)
48	22223	1 (0.4)	102	34412	1 (0.4)	156	55523	1 (0.4)
49	22232	1 (0.4)	103	34434	3 (1.3)	157	55533	2 (0.9)
50	22235	1 (0.4)	104	34443	1 (0.4)	158	55543	1 (0.4)
51	22312	1 (0.4)	105	34445	2 (0.9)	159	55552	1 (0.4)
52	23211	1 (0.4)	106	34452	1 (0.4)	160	55553	2 (0.9)
53	23211	1 (0.4)	107	34454	1 (0.4)	161	55554	1 (0.4)
54	24434	1 (0.4)	108	34533	1 (0.4)	162	55555	2 (0.9)

3.14 Correlation between EQ-5D-5L index and EQ-VAS

There was a significant positive correlation ($r = 0.444$; $P < 0.001$) between the EQ-5D-5L index values and the reported EQ-VAS scores.

3.15 EQ-5D-5L index vs hemoglobin goal

There is a significant association between quality of life and hemoglobin target with p-value 0.039, as shown in table 3.15.

Table 3.15 EQ-5D-5L index vs hemoglobin goal

	Median (IQR)		
	Hb < 11g/dl	**Hb ≥ 11g/dl**	**P-value**
EQ-5D-5L index	0.646 (0.421-0.79)	0.7255 (0.50875-0.823)	0.039

Abbreviation: IQR: Interquartile range, p-value: probability value, Hb: hemoglobin.

Chapter Four
Discussion

Few studies have been established in order to study the management of anemia among patients on HD and its association with HRQOL (Soni et al., 2010, de Goeij et al., 2014).

To the best of our knowledge, this study is the first in Palestine that aimed to provide a baseline data and information that aid to evaluate anemia management in HD patients and its association with HRQOL, patient's demographic and clinical characteristics.

Most of socio-demographic findings of the current study were relatively closed to the results of an observational- retrospective cohort study that was conducted in ten hemodialysis units in the West bank, Palestine in 2015 that aimed to assess the prevalence of drug drug interactions in patients underwent HD (Al-Ramahi et al., 2016); the majority of interviewed patients were male, living in village and married, the average age ± SD was 50.67 ± 15.93 years in the previous study and 51.8% ± 13.9 years in the current study. In addition, 60.2% of patients in the current study were non-smoker whereas 78.9% of patients in the previous study were smoker (Al-Ramahi et al., 2016).

In the current study, most patients had three dialysis sessions per week with a median length 3.5 hours of each session, similar findings were observed with a study conducted on HD patients in Palestine that aimed to define

factors affects quality of life in HD patients (Zyoud et al., 2016); 76.4% of patients received 3 session per week and the session lasts 3 hours in 74.2%.

In the current study hypertension was the most co-comorbid disease in 87.6% of patients followed by DM (56.2%), and the maximum number of medications used by patients was 14, with a mean (± SD) 6.53 ± 2.37. Calcium carbonate was the most common medication used in 85.4% of patients followed by Alfacalclidol (84.1%). In addition the previous study by Al-Ramahi et al., (2016) had comparable findings; where hypertension was the most common co-morbidity (78.5%) followed by DM (42.5%). In addition, number of medications used by patients ranged from one to fifteen medications with a mean (± SD) 7.87 ± 2.44. And Calcium carbonate and Alfacalcidol were the most prescribed medications; 77.1% and 73.8% respectively.

The finding of the current study differs from that of Saudi Arabia study in 2008 and Lebanon study in 2013. In Saudi Arabia, a study by Al-Ageel et al., (2012) enrolled from 87 patients from 2 HD centers over 7 months. In addition, in Lebanon Akel etal., (2017) the study conducted over 6 months between 2013 and 2014. The mean Hb level in our study (10.63 g/dl) was lower than that from Saudi Arabia (11.16 g/dl) and slightly higher than that from Lebanon study (10.29 g/dl). Both Saudi Arabia and Lebanon study measured compliance to KDOQI guideline which define target Hb 11-12 g/dl, however our study define target Hb level 10-11.5 g/dl based on KDIGO 2012 guideline. The percentage of patients with Hb lower than

11g/dl is higher in the current study (59.3%) compared to 45% in Saudi Arabia.

Iron administration in HD patients is frequent, therefore the records for iron status is obligatory for the reason that iron deficiency is contributing to anemia, in addition to hypo responsiveness to ESA. In our study 56.6% of patients received iron therapy, all of them via intravenous route and a dose of 100mg Iron III- hydroxide sucrose. In addition, serum ferritin was recorded for 72.1% of patients, the mean (± SD) concentration for these patients was 447.49± 464.45 ng/ml and 33.1% of them had serum ferritin ≥ 500 ng/ml. Moreover, TSAT was recorded for 81.9% of patients with a mean 32.33 ± 17.16% and 50.3% of them had TSAT ≥ 30%. Whereas in the previous study in Saudi Arabia, 81.6% of patients received iron supplementation all via intravenous route (Al-Ageel et al., 2012). In addition, 55% of patients had serum ferritin concentration recorded with a mean (±SD) 693 ± 420.5ng/ml; and 91.7% of them had serum ferritin ≥ 200ng/ml. Furthermore, 59.8% of patients had TSAT recorded with a mean (±SD) 38± 19.7% and 88.5% of them had TSAT ≥ 20%.

ESA is regularly initiated when Hb level between 9-10 g/dl as recommended by KDIGO, and it suggested not to maintain Hb >11.5g/dl, since increasing Hb >11.5-13g/dl in HD patients may associated with increased impairment such as an increased risk for thrombosis of the vascular access, stroke and hypertension (Cattran et al., 2012, Cases et al., 2018). In this study 37.16% of patients had Hb level < 10g/dl, 2.4% of

them were not initiated the ESA as recommended by KDIGO. Moreover, 24% from 86.7% of patients who received ESA had Hb level > 11.5g/dl, and KDIGO recommended not to maintain the ESA in those patients.

On the other hand, in the current study, the mean (±SD) administered dose of Darbepoetin alpha was 42.1 ± 16.2 mcg. 62.6%, 35.2% and 2.6% of patients who received Darbepoetin were administered 30mcg, 60mcg and 90mcg respectively, once weekly by intravenous route.

In the current study, 76% of patients who received ESA had Hb level ≤ 11.5g/dl, and those require maintaining ESA and should be assessed for ESA hypo responsiveness. Several reasons influence with hypo responssivenes such as iron deficiency, blood loss, noncompliance, infection, inflammation, hyperparathyroidism, inadequate dialysis and bone marrow disorder (Johnson et al., 2007).

Our study shows no significant association between Hb level and any of demographic characteristics documented from patients. The previous study from Saudi Arabia revealed comparable results that there was no significant association between age and Hb level; however, females have statistically significant lower Hb level (Al-Ageel et al., 2012). Also a study conducted in Iran, aimed to assess the adherence to KDOQI guideline and evaluate the relationship between Hb and morbidity (Nafar et al., 2017), showed that younger age was associated with hemoglobin levels lower than 10 g/ dL. On the other hand, a study enrolled 169 patients during 12 months at a single center at Turkey; aimed to determine the factors

affecting Hb variability with inflammatory and nutritional conditions and its associations with all-cause mortality among hemodialysis patients found that the variability in Hb is positively correlated with age (Bal et al., 2018).

On the other hand, the current study demonstrated no significant association between Hb level and number of dialysis session the patients received per week, years of suffering from renal failure, total number of comorbid disease and chronic medications. However, there is a significant association between number of years the patients undergo hemodialysis and hemoglobin target; as patients on chronic hemodialysis become more susceptible to bleeding during dialysis procedure as well as regular blood testing, anticoagulant administration and through intestinal hemorrhage moreover reduced dietary intake duo to diet restriction or loss of appetite all are associated with iron deficiency, consequent anemia and resistance to ESA (Motonishi et al., 2018), (Diebold and Kistler, 2019). However, Al-Ageel et al., (Al-Ageel et al., 2012) revealed no significant association between years of dialysis and Hb level.

By comparing our study with the observational retrospective cohort study that conducted at Hebron governmental hospital during 2014 aimed to evaluate the compliance to treatment guidelines and goals of therapy for diabetes, hypertension, dyslipidemia, bone mineral disorder and anemia, in the mentioned study NKF-KDOQI and KDIGO guidelines were used, the mean Hb level was 8.84 ± 1.52 g/dl, the NKF-KDOQI Hb goals achieved only in 8.9% of patients and regarding to KDIGO goals as stated in their

study 43% of patients had Hb level between 9-11.5g/dl and not exceeded 13g/dl. None of patients had available TSAT and 32.3% had no recorded serum ferritin level. 57.6% and 46.8% had serum ferritin > 200 ng/ml and > 500 ng/ml as recommended by NKF-KDOQI and KDIGO respectively. Iron supplementation used by 69.9% of patients and only 5.1% used ESA as it was not available during the study period due to financial problem at MOH (Al-Ramahi and Namourah, 2016). However, our study showed unlike results by mean Hb level 10.63 ± 1.71 g/dl, Hb goals (10-11.5 g/dl) achieved by 34.1% of patients, moreover 72.1% and 819% of patients had available serum ferritin and TSAT respectively, 33.1% and 50.3% achieved goals of serum ferritin (≥ 500 ng/ml) and TSAT (≥ 30%) respectively. 56.6% of patients received iron replacement and 86.7% received ESA, the reasons for fluctuation between both studies may related to that the previous study conducted over a period by which MOH weren't able to provide ESA therapy as well as performed at one dialysis center (Al-Ramahi and Namourah, 2016).

In the current study the median (interquartile range) of EQ-5D-5L index and EQ-VAS score were 0.69 (0.49-0.81) and 60 (50-75) respectively. While finding of EQ-5D-5L index and EQ-VAS score from a study conducted in Palestine were 0.41 (0.06-0.77) and 50 (50-70) (Zyoud et al., 2016). This difference might be due to the differences in the centers included in both studies. On the other hand, Zyoud et al., (2016) and the current study showed positive correlation between EQ-5D-5L index values and the reported EQ-VAS scores.

Regarding the dimensions of quality of life in this study, 5.3% of patients reported no difficulty in any of the five dimensions; however, 0.9% reported the highest degree of difficulty in the five dimensions. Moreover, the percentage of patients had no problem across the dimension of quality of life mobility, self-care, usual activity, pain/discomfort, and anxiety was as following: 22.6%, 54.9%, 32.3%,29.6% and 25.2% respectively. On the other hand, in the earlier study, Zyoud et al., (2016) found that 6.4% of patients reported no difficulty in any of the five dimensions but 3.4% reported very sever difficulty in the five dimensions. And the percentage of patients had no problem across the dimension of quality of life mobility, self-care, usual activity, pain/discomfort, and anxiety was as following: 27.3%, 54.7%, 37.5%,25.5% and 35.2% respectively (Zyoud et al., 2016).

This study found a significant association between quality of life and hemoglobin target. Similar finding with a study carried out in Iran, aimed to determine the relationship between anemia, HRQOL and some laboratory indices (Sadeghi et al., 2016), showed a significant correlation between Hb and HRQOL. Moreover, a cross sectional study investigated at seven centers in Canada and United states during 2003-2006; aimed to study the relationship between the severity of anemia and quality of life in CKD patients (stage 3-5) by kidney disease quality of life questionnaire (Finkelstein et al., 2009). The study revealed that patients with an increased level of Hb from 11-13 g/dl had a significant improvement in their quality of life. In contrast a cross sectional study conducted in 2007 in Western China investigated HRQOL among hemodialysis patients via EQ-5D-3L,

by which each of 5 dimension has 3 level of no problem, some problem or extreme problem, showed no significant association between EQ-5D score and hemoglobin level (Yuan et al., 2019).

Chapter Five
Conclusion

5.1 Strengths and limitations

To the extent of our knowledge, this research is the first in Palestine regarding studying the management of anemia in HD patients and determination of its association with patient's HRQOL, demographic and clinical characteristics. Furthermore, the data were conducted by face-to-face interview and patients medical record provided comprehensive dependable data.

However, our study had few limitations; First, it's a cross sectional study with short follow up period making the reason and outcome not well established and the resulted associations difficult to be interpreted. Second, the sample size was selected by a convenience sampling technique which may disturb the finding generalizability. Third, as the mainstream data conducted via face-to-face interview, bias could be announced. Although, face-to-face interview provide accurate screening, offer the capture of verbal and non-verbal question that show the level of discomfort with question and capture the behavior and emotions. Lastly some clinical variables such as; parathyroid hormone level, the presence of infection inflammation and blood factors that may be responsible of altering in Hb level and ESA hyporesponsiveness were not determined in our study.

5.2 Conclusion

Our study finds that more than half of patents had Hb level below the target recommended by KDIGO therefore required routinely monitoring of Hb level for early evaluation of anemia. Approximately half of patients received iron replacement supplementation moreover most of them received ESA therapy while only 72.1% and 81.9% of patients had recorded serum ferritin and TSAT respectively, high percentage of patients had Hb level below target unless they received ESA in addition 2.4% of patients had Hb below 10g/dl and did not received ESA, consequently for cost effectiveness and optimal management we need precise defining the underlying causes, choosing the most desirable therapy and regular follow up for assessing the variables associated with inadequate response; recording iron status and Hb level.

Furthermore, our study finds a significant association between Hb level and patients HRQOL, in conclusion, appropriate management of anemia in HD patients by adherence to KDIGO guideline recommendations provides an improvement in their quality of life likewise obtains the optimal therapy.

5.3 Recommendation

- Based on thesis conclusion we recommended routinely assessment of anemia by regular measuring of Hb level among patients on maintaining HD, in addition regular recorded iron status for anemic patients.

- Nephrologist and clinical pharmacist have to select the most effective and suitable treatment approaches and assess patient’s response and express factors related to inadequate response.

- To better understanding the implications of these results, future study could address in Palestine in order to define clinical factors that alter Hb level and responsible for inadequate response.

References

- AKEL, M., SHAMAS, K., SAKR, F., DABBOUS, M., SAFWAN, J., CHERFAN, M. & ISKANDARANI, M. 2017. ***Evaluation of the management of anemia in hemodialysis patients in Lebanon***. **Journal of Nephropharmacology,** 6**,** 68-73.

- AL-AGEEL, N. A., AL-AQEEL, S. A., ABANMY, N. O., ALWAKEEL, J. S., SABRY, A. & ALSARAN, K. A. 2012. A***ppropriateness of anemia management in hemodialysis patients***. **Saudi Pharmaceutical Journal,** 20**,** 85-91.

- AL-ALI, F. S., EL-SAYED ABDELFATTAH, M., FAWZY, A. A., HAMDY, A. F. & ABDULLA, A. E. 2015. ***Erythropoietin-stimulating agents in the management of anemia of end-stage renal disease patients on regular hemodialysis: a prospective randomized comparative study from Qatar*.** **Hemodialysis International**, 19**,** 33-43.

- AL-RAMAHI, R. & NAMOURAH, B. 2016. ***Evaluation of compliance to treatment guidelines and goals of therapy among Palestinian hemodialysis patients***. **Palestinian Medical and Pharmaceutical Journal,** 1**,** 15-24.

- AL-RAMAHI, R., RADDAD, A. R., RASHED, A. O., BSHARAT, A., ABU-GHAZALEH, D., YASIN, E. & SHEHAB, O. 2016. **Evaluation of potential drug- drug interactions among Palestinian hemodialysis patients**. BMC nephrology, 17**,** 96.

- ALLDREDGE, B. K., CORELLI, R. L., ERNST, M. E., GUGLIELMO, B. J., JACOBSON, P. A., KRADJAN, W. A. & WILLIAMS, B. R. 2013. **Koda-Kimble and Young's applied therapeutics: The clinical use of drugs,** Wolters Kluwer Health Adis (ESP).

- ALSUWAIDA, A., ABDULKAREEM, A. & ALWAKEEL, J. 2007. ***The Gulf survey on anemia management (GSAM 2005)***. **Saudi Journal of Kidney Diseases and Transplantation**, 18**,** 206-14.

- BAL, Z., DEMIRCI, B. G., KARAKOSE, S., TUTAL, E., ERKMEN UYAR, M., ACAR, N. O. & SEZER, S. 2018. ***Factors Influencing Hemoglobin Variability and Its Association with Mortality in Hemodialysis Patients.*** **Scientific World Journal,** 2018**,** 8065691.

- CAMERON, J. 1999. **Towards the millennium: a history of renal anaemia and the optimal use of epoetin**. Nephrology Dialysis Transplantation, 14**,** 10-21.

- CASES, A., EGOCHEAGA, M. I., TRANCHE, S., PALLARÉS, V., OJEDA, R., GÓRRIZ, J. L. & PORTOLÉS, J. M. 2018. **Anemia of chronic kidney disease: Protocol of study, management and referral to Nephrology**. Nefrología (English Edition), 38**,** 8-12.

- CATTRAN, D. C., FEEHALLY, J., COOK, H. T., LIU, Z. H., FERVENZA, F. C., MEZZANO, S. A., FLOEGE, J., NACHMAN, P. H., GIPSON, D. S. & PRAGA, M. 2012. **Kidney disease: improving global outcomes (KDIGO) glomerulonephritis work group. KDIGO clinical practice guideline for glomerulonephritis**. Kidney International Supplements, 2**,** 139-274.

- CHAUHAN, R. & MENDONCA, S. 2015. ***Adequacy of twice weekly hemodialysis in end stage renal disease patients at a tertiary care dialysis centre.*** **Indian journal of nephrology,** 25**,** 329.

- DE GOEIJ, M. C., MEULEMAN, Y., VAN DIJK, S., GROOTENDORST, D. C., DEKKER, F. W., HALBESMA, N. & GROUP, P.-S. 2014. **Haemoglobin levels and health-related quality of life in young and elderly patients on specialized predialysis care**. Nephrology Dialysis Transplantation, 29**,** 1391-8.

- DIEBOLD, M. & KISTLER, A. D. 2019. **Evaluation of iron stores in hemodialysis patients on maintenance ferric Carboxymaltose dosing**. BMC nephrology, 20**,** 76.

- EL-ACHKAR, T. M., OHMIT, S. E., MCCULLOUGH, P. A., CROOK, E. D., BROWN, W. W., GRIMM, R., BAKRIS, G. L., KEANE, W. F., FLACK, J. M. & KIDNEY EARLY EVALUATION, P. 2005. H**igher prevalence of anemia with diabetes mellitus in moderate kidney insufficiency: The Kidney Early Evaluation Program**. Kidney international, 67**,** 1483-8.

- EUROQOL GROUP. 2013. **EQ-5D-5L User Guide: Basic information on how to use the EQ-5D-5L instrument [Online].** Available: http://www.euroqol.org/fileadmin/user_upload/Documenten/PDF/Folders_Flyers/UserGuide_EQ-5D-5L_v2.0_October_2013.pdf [Accessed 7 April 2018].

- FINKELSTEIN, F. O., STORY, K., FIRANEK, C., MENDELSSOHN, D., BARRE, P., TAKANO, T., SOROKA, S. & MUJAIS, S. 2009. ***Health-related quality of life and hemoglobin levels in chronic kidney disease patients.*** **Clinical Journal of the American Society of Nephrology**, 4**,** 33-8.

- FISHBANE, S., KOWALSKI, E. A., IMBRIANO, L. J. & MAESAKA, J. K. 1996. ***The evaluation of iron status in hemodialysis patients.*** **Journal of the American Society of Nephrology**, 7**,** 2654-7.

- FISHBANE, S. & MAESAKA, J. K. 1997. I***ron management in end-stage renal disease.*** **American Journal of Kidney Diseases,** 29**,** 319-333.

- FISHBANE, S. & SPINOWITZ, B. 2018. ***Update on Anemia in ESRD and Earlier Stages of CKD: Core Curriculum 2018***. **American Journal of Kidney Diseases**, 71**,** 423-435.

- HIMMELFARB, J. 2005. ***Hemodialysis complications***. **American Journal of Kidney Diseases**, 45**,** 1122-31.

- HSU, C.-Y., BATES, D. W., KUPERMAN, G. J. & CURHAN, G. C. 2001. **Relationship between hematocrit and renal function in men and women.** Kidney international, 59**,** 725-731.

- HSU, C.-Y., MCCULLOCH, C. E. & CURHAN, G. C. 2002. ***Epidemiology of anemia associated with chronic renal insufficiency among adults in the United States: results from the Third National Health and Nutrition Examination Survey***. **Journal of the American Society of Nephrology**, 13**,** 504-510.

- IBRAHIM, S. & EL SALAMONY, O. 2008. ***Depression, quality of life and malnutrition-inflammation scores in hemodialysis patients***. **American journal of nephrology,** 28**,** 784-91.

- JACOBS, C., FREI, D. & PERKINS, A. C. 2005a. **Results of the European Survey on Anaemia Management 2003 (ESAM 2003): current status of anaemia management in dialysis patients, factors affecting epoetin dosage and changes in anaemia management over the last 5 years.** Nephrology Dialysis Transplantation, 20 Suppl 3**,** iii3-24.

- JACOBS, C., FREI, D. & PERKINS, A. C. 2005b. **Results of the European Survey on Anaemia Management 2003 (ESAM 2003): current status of anaemia management in dialysis patients, factors affecting epoetin dosage and changes in anaemia management over the last 5 years**. Nephrology Dialysis Transplantation, 20**,** iii3-iii24.

- JIANG, J. L., REN, W., SONG, J., SUN, Q. L., XIAO, X. Y., DIAO, X. Z., HUANG, Y. H., LAN, L., WANG, P. & HU, Z. 2013. ***The impact of short daily hemodialysis on anemia and the quality of life in Chinese patients***. **Brazilian Journal of Medical and Biological Research**, 46**,** 629-33.

- JOHNSON, D. W., POLLOCK, C. A. & MACDOUGALL, I. C. 2007. **Erythropoiesis-stimulating agent hyporesponsiveness**. Nephrology (Carlton), 12**,** 321-30.

- KDIGO BOARD MEMBERS 2012. **Kidney disease: Improving global outcomes (KDIGO) clinical practice guideline for anemia in chronic kidney disease.** Official Journal of the International Society of Nephrology, 2**,** 279-335.

- KLIGER, A. S., FOLEY, R. N., GOLDFARB, D. S., GOLDSTEIN, S. L., JOHANSEN, K., SINGH, A. & SZCZECH, L. 2013. KDOQI US ***commentary on the 2012 KDIGO Clinical Practice Guideline for Anemia in CKD***. **American Journal of Kidney Diseases**, 62**,** 849-59.

- LEVEY, A. S. & CORESH, J. 2012. **Chronic kidney disease**. Lancet, 379**,** 165-80.

- LOPES, A. A., BRAGG, J., YOUNG, E., GOODKIN, D., MAPES, D., COMBE, C., PIERA, L., HELD, P., GILLESPIE, B. & PORT, F. K. 2002. **Depression as a predictor of mortality and hospitalization among hemodialysis patients in the United States and Europe**. Kidney international, 62**,** 199-207.

- MAPES, D. L., LOPES, A. A., SATAYATHUM, S., MCCULLOUGH, K. P., GOODKIN, D. A., LOCATELLI, F., FUKUHARA, S., YOUNG, E. W., KUROKAWA, K. & SAITO, A. 2003. **Health-related quality of life as a predictor of mortality and hospitalization: the Dialysis Outcomes and Practice Patterns Study (DOPPS).** Kidney international, 64**,** 339-349.

- MOTONISHI, S., TANAKA, K. & OZAWA, T. 2018. **Iron deficiency associates with deterioration in several symptoms independently from hemoglobin level among chronic hemodialysis patients.** PloS one, 13.

- MUJAIS, S. K., STORY, K., BROUILLETTE, J., TAKANO, T., SOROKA, S., FRANEK, C., MENDELSSOHN, D. & FINKELSTEIN, F. O. 2009. ***Health-related quality of life in CKD Patients: correlates and evolution over time***. **Clinical Journal of the American Society of Nephrology**, 4**,** 1293-301.

- MURTAGH, F. E., ADDINGTON-HALL, J. & HIGGINSON, I. J. 2007. **The prevalence of symptoms in end-stage renal disease: a systematic review.** Adv Chronic Kidney Dis, 14**,** 82-99.

- NAFAR, M., SAMAVAT, S., KHOSHDEL, A. & ALIPOUR-ABEDI, B. 2017. ***Anemia Evaluation and Erythropoietin Dose Requirement Among Hemodialysis Patients***. **Iranian journal of kidney diseases**, 11.

- ORNT, D. B., LARIVE, B., RASTOGI, A., RASHID, M., DAUGIRDAS, J. T., HERNANDEZ, A., KURELLA TAMURA, M., SURI, R. S., LEVIN, N. W., KLIGER, A. S. & FREQUENT HEMODIALYSIS NETWORK TRIAL, G. 2013. I**mpact of frequent hemodialysis on anemia management: results from the Frequent Hemodialysis Network (FHN) Trials**. Nephrology Dialysis Transplantation, 28**,** 1888-98.

- PALESTINIAN MINISTRY OF HEALTH. 2016. **Health Annual Report - Palestine 2015 [Online]**. Available: http://www.moh.ps/mohsite/Content/Books/NWNJXX7RJ92Bn4f5EGYiH43a2tjAAzKBnseGnEUCaqWqYZndsbCcPy_JQWguvkHTR4Xk4zUpdT45ooWxH11BhIbVAxwpGWy2wiwHdGcM5K7aZ.pdf [Accessed 7 April 2018].

- PALESTINIAN MINISTRY OF HEALTH. 2017. Health Annual report - Palestine 2016 [Online]. Available: http://www.moh.ps/mohsite/Content/Books/ZxRcynmiUofNqt66u4CrHRgmJR6Uv7z77srjjIEAho6xnz5V3rgLTu_RhO7xf2j2VusNiIvWkjwp84yXHLdGleB97gKrHHI5iZ9oPJ25owGEN.pdf [Accessed 7 April 2018].

- PISONI, R. L., BRAGG-GRESHAM, J. L., YOUNG, E. W., AKIZAWA, T., ASANO, Y., LOCATELLI, F., BOMMER, J., CRUZ, J. M., KERR, P. G., MENDELSSOHN, D. C., HELD, P. J. & PORT, F. K. 2004. ***Anemia management and outcomes from 12 countries in the Dialysis Outcomes and Practice Patterns Study (DOPPS)***. **American Journal of Kidney Diseases,** 44**,** 94-111.

- SADEGHI, M., EBRAHIMI, H., ABBASI, M. & NOROUZADEH, R. 2016. ***Relationship between anemia, quality of life, and laboratory indices in hemodialysis patients***. **Saudi Journal of Kidney Diseases and Transplantation,** 27**,** 1063.

- SEICA, A., SEGALL, L., VERZAN, C., VADUVA, N., MADINCEA, M., RUSOIU, S., CRISTEA, S., STEFAN, M., SERBANESCU, D., MOROSANU, P., GRAJDEANU, L., ANDRONACHE, R., NECHITA, M., DRAGOS, D., DRONCA, A., GUSBETH-TATOMIR, P., MIRCESCU, G. & COVIC, A. 2009. **Factors affecting the quality of life of haemodialysis patients from Romania: a multicentric study**. Nephrology Dialysis Transplantation, 24**,** 626-9.

- SINGH, A. K., SZCZECH, L., TANG, K. L., BARNHART, H., SAPP, S., WOLFSON, M., REDDAN, D. & INVESTIGATORS, C. 2006. **Correction of anemia with epoetin alfa in chronic kidney disease**. N Engl J Med, 355**,** 2085-98.

- SONI, R. K., WEISBORD, S. D. & UNRUH, M. L. 2010. **Health-related quality of life outcomes in chronic kidney disease**. Current opinion in nephrology and hypertension, 19**,** 153-9.

- STRIPPOLI, G. F. & CLINICAL EVALUATION OF THE, D. O. E. S. G. 2010. **Effects of the dose of erythropoiesis stimulating agents on cardiovascular events, quality of life, and health-related costs in hemodialysis patients: the clinical evaluation of the dose of erythropoietins (C.E. DOSE) trial protocol.** Trials, 11**,** 70.

- THOMAS, R., KANSO, A. & SEDOR, J. R. 2008. **Chronic kidney disease and its complications.** Prim Care, 35**,** 329-44, vii.

- VAN, D. W. I**ron deficiency in patients with dialysis-associated anemia during erythropoietin replacement therapy: strategies for assessment and management.** Seminars in Nephrology, 1989. 21-24.

- VAN WYCK, D. B., STIVELMAN, J. C., RUIZ, J., KIRLIN, L. F., KATZ, M. A. & OGDEN, D. A. 1989. **Iron status in patients receiving erythropoietin for dialysis-associated anemia**. Kidney international, 35**,** 712-6.

- WANG, W., KNOVICH, M. A., COFFMAN, L. G., TORTI, F. M. & TORTI, S. V. 2010. **Serum ferritin: past, present and future**. Biochim Biophys Acta, 1800**,** 760-9.

- WORWOOD, M. & MAY, A. 2006. **Iron deficiency anaemia and iron overload.** Dacie and Lewis practical haematology. 10th ed. Philadelphia: Church Livingstone Elsevier**,** 131-60.

- YUAN, H., YANG, Y., ZHANG, Y., XUE, G. & CHEN, L. 2019. ***The health-related quality of life among patients on maintenance haemodialysis: evaluation using the EQ-5D***. **Journal of clinical nursing**.

- ZUO, L., WANG, M., HOU, F., YAN, Y., CHEN, N., QIAN, J., WANG, M., BIEBER, B., PISONI, R. L., ROBINSON, B. M. & ANAND, S. 2016. **Anemia Management in the China Dialysis Outcomes and Practice Patterns Study**. Blood purification, 42**,** 33-43.

- ZYOUD, S. H., DARAGHMEH, D. N., MEZYED, D. O., KHDEIR, R. L., SAWAFTA, M. N., AYASEH, N. A., TABEEB, G. H., SWEILEH, W. M., AWANG, R. & AL-JABI, S. W. 2016. **Factors affecting quality of life in patients on haemodialysis: a cross-sectional study from Palestine.** BMC nephrology, 17**,** 44.

Appendices

Appendix 1

2012 KDIGO Guideline

Table 1.1: 2012 KDIGO recommendation for diagnosis of anemia

(KDIGO Board Members, 2012)

1.2.1:	Diagnose anemia in adults and children >15 years with CKD when the Hb concentration is <13.0 g/dl (<130 g/l) in males and <12.0 g/dl (<120 g/l) in females. (Not Graded)
1.2.2:	Diagnose anemia in children with CKD if Hb concentration is <11.0 g/dl (<110 g/l) in children 0.5–5 years, <11.5 g/dl (115 g/l) in children 5–12 years, and <12.0 g/dl (120 g/l) in children 12–15 years. (Not Graded)

Table 1.2: 2012 KDIGO recommendations for use of iron supplementation in patients with CKD. (KDIGO Board Members, 2012)

2.1.1:	When prescribing iron therapy, balance the potential benefits of avoiding or minimizing blood transfusions, ESA therapy, and anemia related symptoms against the risks of harm in individual patients (e.g., anaphylactoid and other acute reactions, unknown long-term risks). (Not Graded)
2.1.2:	For adult CKD patients with anemia not on iron or ESA therapy we suggest a trial of IV iron (or in CKD ND patients alternatively a 1–3 month trial of oral iron therapy) if (2C): • an increase in Hb concentration without starting ESA treatment is desired* and • TSAT is ≤30% and ferritin is ≤500 ng/ml (≤500 mg/l)
2.1.3:	For adult CKD patients on ESA therapy who are not receiving iron supplementation, we suggest a trial of IV iron (or in CKD ND patients alternatively a 1–3 month trial of oral iron therapy) if (2C): • an increase in Hb concentration** or a decrease in ESA dose is desired*** and • TSAT is ≤30% and ferritin is ≤500 ng/ml (≤500 mg/l)
2.1.4:	For CKD ND patients who require iron supplementation, select the route of iron administration based on the severity of iron deficiency, availability of venous access, response to prior oral iron therapy, side effects with prior oral or IV iron therapy, patient compliance, and cost. (Not Graded)
2.1.5:	Guide subsequent iron administration in CKD patients based on Hb responses to recent iron therapy, as well as ongoing blood losses, iron status tests (TSAT and ferritin), Hb concentration, ESA responsiveness and ESA dose in ESA treated patients, trends in each parameter, and the patient's clinical status. (Not Graded)
2.1.6:	For all pediatric CKD patients with anemia not on iron or ESA therapy, we recommend oral iron (or IV iron in CKD HD patients) administration when TSAT is ≤20% and ferritin is ≤100 ng/ml (≤100 lg/l). (1D)
2.1.7:	For all pediatric CKD patients on ESA therapy who are not receiving iron supplementation, we recommend oral iron (or IV iron in CKD HD patients) administration to maintain TSAT >20% and ferritin >100 ng/ml (>100 lg/l). (1D)
	*Based on patient symptoms and overall clinical goals, including avoidance of transfusion, improvement in anemia-related symptoms, and after exclusion of active infection. **Consistent with Recommendations #3.4.2 and 3.4.3. ***Based on patient symptoms and overall clinical goals including avoidance of transfusion and improvement in anemia-related symptoms, and after exclusion of active infection and other causes of ESA hyporesponsiveness.

Table 1.3: 2012 KDIGO recommendations for use of ESAs and other agents to treat anemia in CKD: ESA initiation (KDIGO Board Members, 2012)

3.1:	Address all correctable causes of anemia (including iron deficiency and inflammatory states) prior to initiation of ESA therapy. (Not Graded)
3.2:	In initiating and maintaining ESA therapy, we recommend balancing the potential benefits of reducing blood transfusions and anemia-related symptoms against the risks of harm in individual patients (e.g., stroke, vascular access loss, hypertension). (1B)
3.3:	We recommend using ESA therapy with great caution, if at all, in CKD patients with active malignancy—in particular when cure is the anticipated outcome—(1B), a history of stroke (1B), or a history of malignancy (2C).
3.4.1:	For adult CKD ND patients with Hb concentration ≥10.0 g/dl (≥100 g/l), we suggest that ESA therapy not be initiated. (2D)
3.4.2:	For adult CKD ND patients with Hb concentration <10.0 g/dl (<100 g/l) we suggest that the decision whether to initiate ESA therapy be individualized based on the rate of fall of Hb concentration, prior response to iron therapy, the risk of needing a transfusion, the risks related to ESA therapy and the presence of symptoms attributable to anemia. (2C)
3.4.3:	For adult CKD 5D patients, we suggest that ESA therapy be used to avoid having the Hb concentration fall below 9.0 g/dl (90 g/l) by starting ESA therapy when the hemoglobin is between 9.0–10.0 g/dl (90–100 g/l). (2B)
3.4.4:	Individualization of therapy is reasonable as some patients may have improvements in quality of life at higher Hb concentration and ESA therapy may be started above 10.0 g/dl (100 g/l). (Not Graded)
3.4.5:	For all pediatric CKD patients, we suggest that the selection of Hb concentration at which ESA therapy is initiated in the individual patient includes consideration of potential benefits (e.g., improvement in quality of life, school attendance/performance, and avoidance of transfusion) and potential harms. (2D)

Table 1.4: 2012 KDIGO recommendations for use of ESAs and other agents to treat anemia in CKD: ESA maintenance therapy (KDIGO Board Members, 2012)

3.5.1:	In general, we suggest that ESAs not be used to maintain Hb concentration above 11.5 g/dl (115 g/l) in adult patients with CKD. (2C)
3.5.2:	Individualization of therapy will be necessary as some patients may have improvements in quality of life at Hb concentration above 11.5 g/dl (115 g/l) and will be prepared to accept the risks. (Not Graded)
3.6:	In all adult patients, we recommend that ESAs not be used to intentionally increase the Hb concentration above 13 g/dl (130 g/l). (1A)
3.7:	In all pediatric CKD patients receiving ESA therapy, we suggest that the selected Hb concentration be in the range of 11.0 to 12.0 g/dl (110 to 120 g/l). (2D)

Table 1.5: 2012 KDIGO recommendations for use of ESAs and other agents to treat anemia in CKD: ESA dosing, administration and frequency. (KDIGO Board Members, 2012)

3.8.1:	We recommend determining the initial ESA dose using the patient's Hb concentration, body weight, and clinical circumstances. (1D)
3.8.2:	We recommend that ESA dose adjustments be made based on the patient's Hb concentration, rate of change in Hb concentration, current ESA dose and clinical circumstances. (1B)
3.8.3:	We suggest decreasing ESA dose in preference to withholding ESA when a downward adjustment of Hb concentration is needed. (2C)
3.8.4:	Re-evaluate ESA dose if (Not Graded): • The patient suffers an ESA-related adverse event • The patient has an acute or progressive illness that may cause ESA hyporesponsiveness (See Recommendations 3.13.1–3.13.2)
3.9.1:	For CKD 5HD patients and those on hemofiltration or hemodiafiltration therapy, we suggest either intravenous or subcutaneous administration of ESA. (2C)
3.9.2:	For CKD ND and CKD 5PD patients, we suggest subcutaneous administration of ESA. (2C)
3.10:	We suggest determining the frequency of ESA administration based on CKD stage, treatment setting, efficacy considerations, patient tolerance and preference, and type of ESA. (2C)

Appendix 2

Data Collection Form

An- Najah National University

Data Collection Form

A. Patient demographic characteristics

A.1 Patient number: _____

A.2 Date of birth: ____/_____/_____

A.3 Age: _____ years

A.4 Gender: □ Male □ Female

A.5Weight: _____ Kg

A.6Height: _____ cm

A.7 Level of education:

□ Illiterate □ Primary □ Secondary □ University □Postgraduate

A.8 Income:

□ Low (Less than 2000 NIS)

□ Moderate (2000-5000 NIS)

□ High (More than 5000 NIS)

A.9 Marital Status:

□ Married □ Single □ Divorced □ Widowed

A. 10 Locality:

□ Urban □ Rural □ Camp

A.11 Employment status

□ Unemployed □ Employed □ Previously employed before failure onset

A.12 Family history of Renal Failure:

□ Yes □ No

B. History and disease co-morbidities

B.1 Number of dialysis per week: _____

B.2 How many years do you suffer from Renal Failure: _____

B.3How many years do you undergo dialysis: _____

B.4 How many hours does the session of dialysis continue: _____

B.5: Smoking

□ Current smoking

□ Previous smoker but non current smoking

□ Non-smoker

Years of Smoking: _____

B.6: Do you make exercises

□ Yes

□ No

How many times weekly: _____

B.7. Do you use any herbal remedies?

□ Yes Mention: _____

□ No

B.8: Co-morbidities:

□ Hypertension

□ Dyslipidemia

□Heart failure

□Nephrotoxicity

□Systemic infection

□Anemia

□ Ischemic heart disease

□ Diabetes mellitus

□ Atrial fibrillation

□ Polycystic Kidney Disease

□ UTI

□ Urinary Stones

□ Hyperparathyroidism

□ Others : …….

C. Management and Medications

C.1: Medications

Drug name	Drug dose	Frequency	Route	Day of Dialysis

C.2: Laboratory Tests

Test	Date	Result	Normal Range
Hemoglobin (Hb)			
Hematocrit (HCT)			
Transferrin saturation (TSAT)			
Serum ferritin			
Iron, Total			
Total Iron Binding Capacity (TIBC)			
Serum Creatinine			
Albumin			
Sodium			
Potassium			
Calcium			
Phosphorous			
Fasting Blood Glucose (FBG)			
Random Blood Glucose (RBG)			
Bilirubin, Total			
Blood Urea Nitrogen (BUN)			
C-Reactive protein (CRP)			

Quality of life:

ضع علامة في المربع الخاص بكل مجموعة في الأسفل، لتشير إلى أفضل عبارة تصف حالتك الصحية اليوم.

1- القدره على التنقل:

- ☐ **ليس لدي أي مشاكل عند المشي**
- ☐ **أعاني من مشاكل طفيفة عند المشي**
- ☐ **أعاني من مشاكل متوسطة عند المشي**
- ☐ **أعاني من مشاكل حادة عند المشي**
- ☐ **ليس لدي القدره على المشي**

2- قدرتي على الاهتمام بنفسي:

- ☐ **ليس لدي أي مشاكل في الاستحمام أوارتداء ملابسي بنفسي**
- ☐ **أعاني من مشاكل طفيفة في الاستحمام أوارتداء الملابس بنقسي**
- ☐ **أعاني من مشاكل متوسطة عند الاستحمام أو ارتداء الملابس بنفسي**
- ☐ **أعاني من مشاكل حادة عند الاستحمام أو ارتداء الملابس بنفسي**
- ☐ **ليس لدي القدرة على الاستحمام أو ارتداء الملابس بنفسي**

3- الأنشطة المعتادة (مثل العمل، الدراسة، الأعمال المنزلية، النشاطات الأسرية أوالترفيهية):

- ☐ **ليس لدي أي مشاكل في ممارسة نشاطاتي المعتادة**
- ☐ **أعاني من مشاكل طفيفة في القيام بنشاطاتي المعتادة**
- ☐ **أعاني من مشاكل متوسطة في ممارسة نشاطاتي المعتادة**
- ☐ **أعاني من مشاكل حادة في ممارسة نشاطاتي المعتادة**
- ☐ **ليس لديّ القدرة على ممارسة نشاطاتي المعتادة**

4- **الألم/الإحساس بعدم الراحة:**

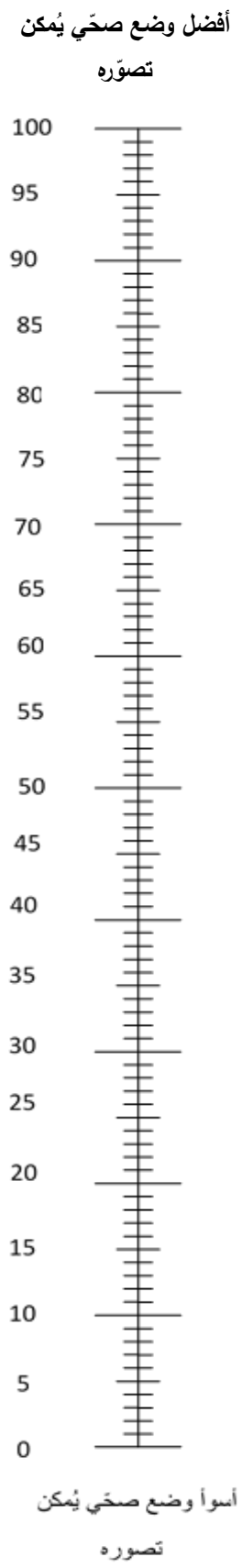
- ☐ **ليس لدي أي ألم أو انزعاج**
- ☐ **أعاني من ألم طفيف أو انزعاج طفيف**
- ☐ **أعاني من ألم متوسط أو انزعاج متوسط**
- ☐ **أعاني من ألم حاد أو انزعاج حاد**
- ☐ **أعاني من ألم شديد جداً أو انزعاج شديد جداً**

5- قلق / اكتئاب:

- ☐ **لا أعاني من أي قلق أو اكتئاب**
- ☐ **أعاني من قلق طفيف أو اكتئاب طفيف**
- ☐ **أعاني من قلق متوسط أو اكتئاب متوسط**
- ☐ **أعاني من قلق حاد أو اكتئاب حاد**
- ☐ **أعاني من قلقاً شديداً جداً أو اكتئاباً شديداً جداً**

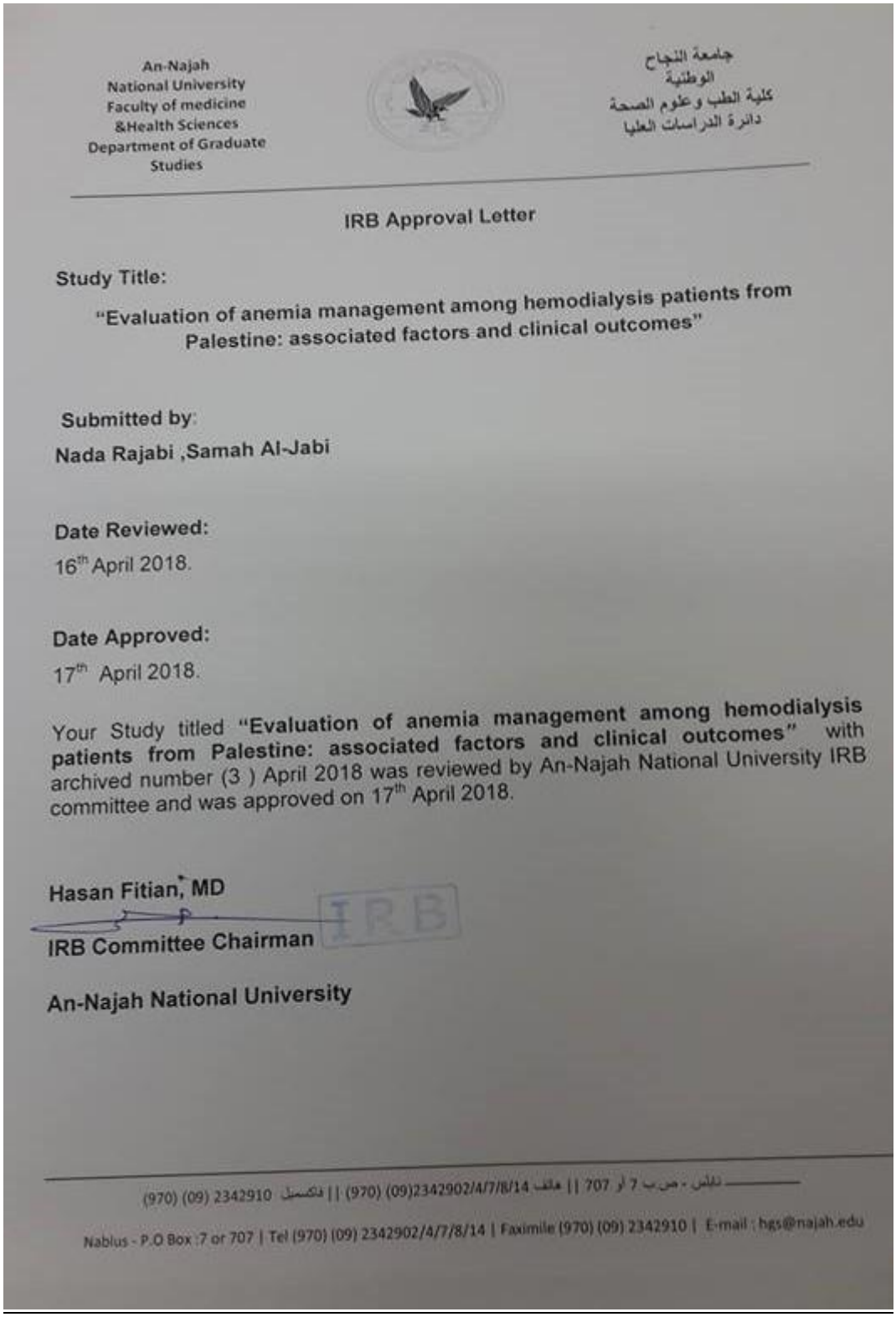
- **نود أن نعرف مدى جودة أو سوء صحتك اليوم.**
- **هذا المقياس مدرج من الرقم 0 حتى 100.**
- **الرقم 100 يعني أحسن حالة صحية يمكنك تصوّرها.**

  0 يعني أسوأ حالة صحية يمكنك تصوّرها.
- **ضع X على المقياس للإشارة إلى وضعك الصحي اليوم.**
- **الآن، قم رجاء بكتابة الرقم الذي أشرت إليه على المقياس في الصندوق أدناه.**
- **حالتك الصحية اليوم =**



Appendix 3

Institutional Review Board Approval Letter



An-Najah
National University
Faculty of medicine
&Health Sciences
Department of Graduate
Studies

جامعة النجاح
الوطنية
كلية الطب وعلوم الصحة
دائرة الدراسات العليا

IRB Approval Letter

Study Title:

"Evaluation of anemia management among hemodialysis patients from Palestine: associated factors and clinical outcomes"

Submitted by:

Nada Rajabi ,Samah Al-Jabi

Date Reviewed:

16th April 2018.

Date Approved:

17th April 2018.

Your Study titled **"Evaluation of anemia management among hemodialysis patients from Palestine: associated factors and clinical outcomes"** with archived number (3) April 2018 was reviewed by An-Najah National University IRB committee and was approved on 17th April 2018.

Hasan Fitian, MD

IRB Committee Chairman

An-Najah National University

IRB

(970) (09) 2342910 فاكسميل || (970) (09)2342902/4/7/8/14 هاتف || نابلس - ص.ب 7 أو 707

Nablus - P.O Box :7 or 707 | Tel (970) (09) 2342902/4/7/8/14 | Faximile (970) (09) 2342910 | E-mail : hgs@najah.edu

Appendix 4

Ministry of Health Approval Letter

State of Palestine
Ministry of Health - Nablus
General Directorate of Education in Health

دولة فلسطين
وزارة الصحة- نابلس
الإدارة العامة للتعليم الصحي

Ref.: .....
Date: .....

الرقم: ٢٠١٨/٦٥٨/١٦٢
التاريخ: ٢٠١٨/٥/٢٤

الأخ مدير عام الادارة العامة للمستشفيات المحترم،،،

الأخ مدير مجمع فلسطين الطبي المحترم،،،

تحية واحترام،،

الموضوع: تسهيل مهمة طالبة ماجستير – جامعة النجاح

يرجى تسهيل مهمة الطالبة: ندى صادق عبد الرحمن رجبي- ماجستير صيدلة سريرية/ جامعة النجاح، في عمل بحث بعنوان "تقييم علاج فقر الدم لمرضى غسيل الكلى من فلسطين: العوامل المرتبطة والنتائج السريرية"، من خلال السماح للطالبة بجمع معلومات من خلال مراجعة ملفات المرضى ومقابلة المرضى (بعد اخذ موافقتهم) لجمع معلومات تتعلق بالبحث، وذلك في:

- مستشفى بيت جالا الحكومي
- مجمع فلسطين الطبي

علما أن البحث تحت اشراف د. سماح الجابي. كما انه سيتم الالتزام بمعايير البحث العلمي والحفاظ على سرية المعلومات.

مع الاحترام،،

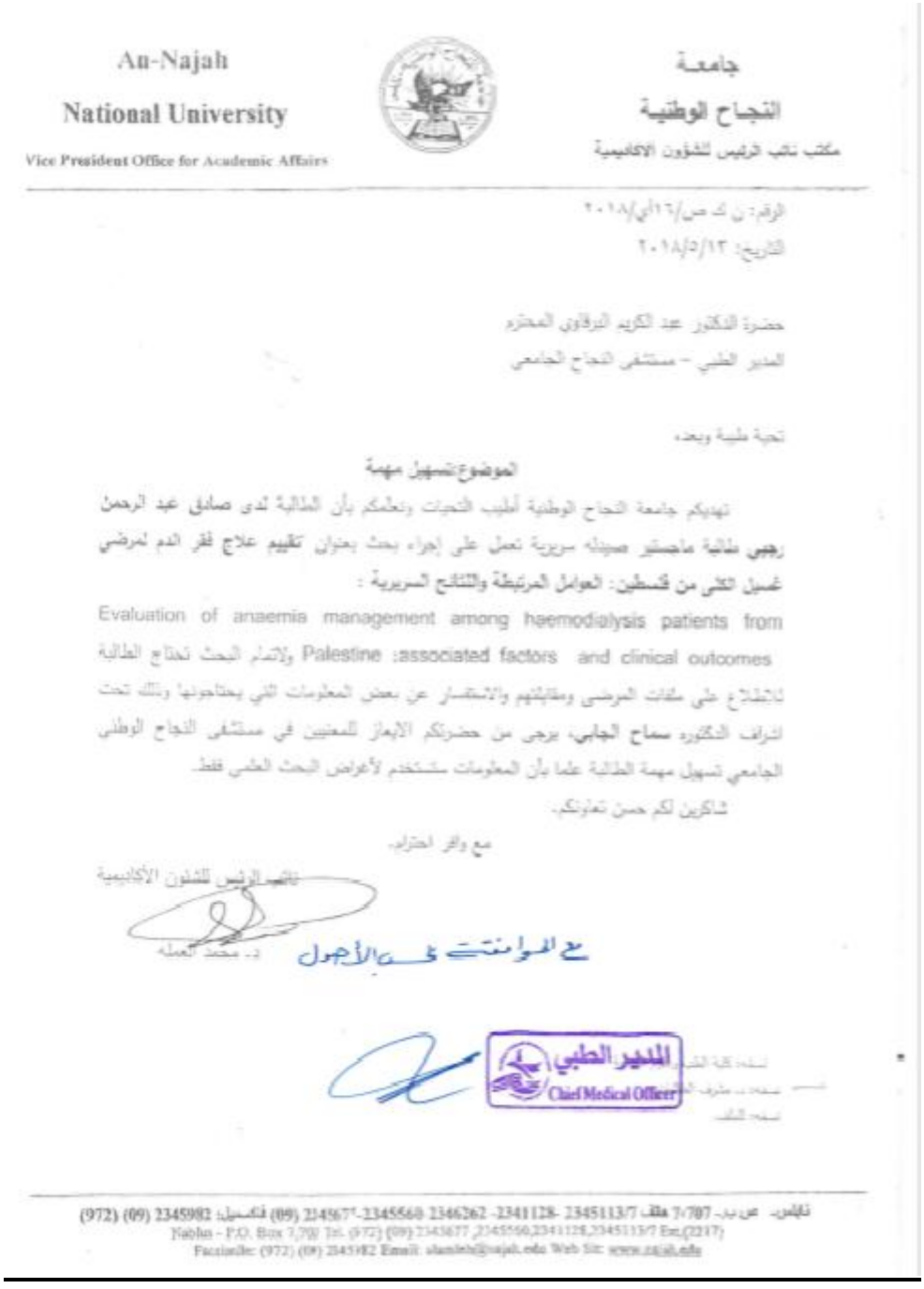
وزارة فلسطين الصحة
د. أمل أبو عوض
الإدارة العامة للتعليم الصحي

مدير عام التعليم الصحي

نسخة: نائب الرئيس للشؤون الأكاديمية المحترم/ جامعة النجاح

Appendix 5

An-Najah National University Hospital Approval Letter



An-Najah
National University
Vice President Office for Academic Affairs

جامعة
النجاح الوطنية
مكتب نائب الرئيس للشؤون الاكاديمية

الرقم: ن ك ص/١٦أ/٢٠١٨
التاريخ: ١٣/٥/٢٠١٨

حضرة الدكتور عبد الكريم البرقاوي المحترم
المدير الطبي – مستشفى النجاح الجامعي

تحية طيبة وبعد،

الموضوع: تسهيل مهمة

تهديكم جامعة النجاح الوطنية أطيب التحيات وتعلمكم بأن الطالبة لدى صادق عبد الرحمن رجبي طالبة ماجستير صيدلة سريرية تعمل على إجراء بحث بعنوان تقييم علاج فقر الدم لمرضى غسيل الكلى من فلسطين: العوامل المرتبطة والنتائج السريرية :

Evaluation of anaemia management among haemodialysis patients from Palestine :associated factors and clinical outcomes

ولإتمام البحث تحتاج الطالبة للاطلاع على ملفات المرضى ومقابلتهم والاستفسار عن بعض المعلومات التي يحتاجونها وذلك تحت اشراف الدكتوره سماح الجابي، يرجى من حضرتكم الايعاز للمعنيين في مستشفى النجاح الوطني الجامعي تسهيل مهمة الطالبة علما بأن المعلومات ستستخدم لأغراض البحث العلمي فقط.

شاكرين لكم حسن تعاونكم.

مع وافر احترام،

نائب الرئيس للشؤون الأكاديمية
د. محمد العملة

مع الموافقة على الأصول

المدير الطبي
Chief Medical Officer

نابلس- ص.ب. 7/707 هاتف 2345982 (09) 2345677-2345560 2346262 -2341128- 2345113/7 فاكسميل: (972) (09) 2345982
Nablus - P.O. Box 7/707 Tel. (972) (09) 2345677 ,2345560,2341128,2345113/7 Ext.(2217)
Facsimile: (972) (09) 2345982 Email: vhamleh@najah.edu Web Site: www.najah.edu

جامعة النجاح الوطنية

كلية الدراسات العليا

تقييم علاج فقر الدم عند مرضى غسيل الكلى في فلسطين: العوامل المرتبطة والنتائج السريرية

اعداد

ندى صادق رجبي

اشراف

الدكتورة سماح الجابي

قدمت هذه الاطروحة استكمالاً لمتطلبات الحصول على درجة الماجستير في الصيدلة السريرية، بكلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس – فلسطين.

2020

تقييم علاج فقر الدم عند مرضى غسيل الكلى في فلسطين: العوامل المرتبطة والنتائج السريرية

إعداد

ندى صادق رجبي

اشراف

د. سماح الجابي

الملخص

الخلفية: يعتبر فقر الدم من المضاعفات المتكررة لدى مرضى غسيل الكلى. الرعاية المناسبة هي التي تتضمن اعطاء المريض مكملات الحديد والأدوية التى تعمل على تحفيز الإريثروبويتين (ESA)، اضافة إلى جانب مراقبة استجابه جسم المريض للعلاج. ان سوء جوده الحياة الصحية هي من المضاعفات الشائعة عند هولاء المرضى وتكون ناتجة عن عملية غسيل الكلى نفسها أو مضاعفاتها.

الأهداف: تهدف هذه الدراسة إلى تقييم علاج فقر الدم لدى مرضى غسيل الكلى في فلسطين، تحديد الخصائص الديموغرافية والسريرية المرتبطة به، وتقييم جودة الحياة الصحية وارتباطها مع علاج فقر الدم المناسب.

المنهجية: هذه الدراسة عبارة عن دراسة وصفية. تم تطبيقها في ثلاثة مراكز لغسيل الكلى في الضفة الغربية – فلسطين خلال الفترة من 24 يونيو إلى 5 سبتمبر 2018. تم ملئ البيانات عن طريق إجراء مقابلات مع المرضى ومن الملفات الشخصية الصحية لهم. يتكون نموذج جمع البيانات من جزئين، يحتوي الأول على معلومات ديموغرافية وسريرية حول المرضى، بينما يحتوي الجزء الثاني على مؤشرEQ-5D لتقييم جودة الحياة وEQ-VAS الذي يقيم الحالة الصحية الحالية للمرضى من وجهه نظرهم.

النتائج: شارك في الدراسة 226 مريضا. وكان متوسط عمر المرضى 13.9 ± 57 سنة. ومتوسط مستوى الهيموغلوبين 1.7 ± 10.63 غم/ مل. 34.1٪ من المرضى لديهم مستوى هيموغلوبين 11.5–10 غم/ مل. فقط 72.1٪ و81.9٪ من المرضى توفرت لديهم قياسات

الفيريتين في الدم وتشبع الترانسفيرين على التوالي. وكذلك 33.1٪ من المرضى كانت لهم نسبه الفيريتين في الدم ≤ 500 نانوغرام/ مل و50.3٪ كانت لهم نسبة تشبع الترانسفيرين ≤ 30%. جميع المرضى الذين تلقوا مكملات الحديد تلقوها عن طريق الوريد وبجرعة 100 مغ من iron sucrose. علاج Darbepoetin استخدم عند 86.7٪ من المرضى عن طريق الوريد والجرعة الأسبوعية كانت 0.45 ميكروغرام /كغم. كذلك 24٪ منهم لديهم نسبه هيموغلوبين أعلى من 11.5 غم/مل. من بين المرضى الذين كان لديهم نسبة هيموغلوبين أقل من 10 غم/مل كان 2.4٪ منهم لم يتلقوا علاج ESA. فيما يتعلق بجودة الحياه الصحية عند المرضى كان 22.6٪، 54.9٪، 32.3٪، 29.6٪ و25.2٪ منهم ليس لديهم أي مشاكل متعلقة في قدرتهم على التنقل، الاهتمام بانفسهم، ممارسه الانشطة المعتادة، الألم /الاحساس بعدم الراحة والانزعاج والقلق على التوالي. 0.9٪ فقط من المرضى سجل لديهم أعلى درجة من الصعوبة في كل من الأبعاد الخمسة. كان هناك ارتباط كبير بين مستوى الهيموغلوبين وعدد السنوات التي تلقى فيها المرضى غسيل الكلى ومع جودة الحياة الصحية للمرضى.

الخلاصة: توصلت الدراسة إلى وجود ارتباط كبير بين مستوى الهيموغلوبين وجودة الحياة الصحية للمرضى، وبالتالي فإن الرعاية المناسبة لفقر الدم لدى مرضى غسيل الكلى من خلال الالتزام بتوصيات KDIGO التوجيهية سوف توفر تحسنا في جودة حياتهم إضافة إلى الحصول على العلاج الأمثل.