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RESEARCH ARTICLE

Phosphate Binder's Adherence and Knowledge among Hemodialysis Patients in Karbala Center, Cross-Sectional Study

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ABSTRACT

Among patients with end stage renal disease (ESRD), the Non-adherence to phosphate binder medications represents a big contributor for hyperphosphatemia management failure. Hence, it makes the patient prone for high risk of cardiovascular morbidity and all-cause mortality as a consequence of hyperphosphatemia. Thus, we tend in this study to investigate whether there is an association between adherence, knowledge, serum phosphate, and any of patient demographic characteristics affecting phosphate binder adherence. This study is a cross sectional, descriptive, single arm study for the purpose of evaluating the patient adherence and knowledge toward phosphate binder medications in hemodialysis patients with hyperphosphatemia. This study was conducted at the dialysis Centers in Al_Imam Al Hussein Teaching Hospital. All participating patients were asked to answer two questionnaires [Patient Knowledge questionnaire and Morisky Medication Adherence Scale]. 204 patients participate in the study where the percentage of residence from inside of Karbala was 97.5 %. The study shows the major cause of chronic kidney disease in most patient was hypertension with percentage (N=70, 34.3%), followed by diabetes mellitus by 15.7%. About knowledge, 58% answered accurately about phosphate binders' indication. In regard to the question, ''When should you take your phosphate binder?' 37.2% responded true and around 95% give inappropriate answer about the question' 'What should you do if you have forgotten to take your phosphate binder? ''58% of patients didn't know if there's side effect for phosphate binders or not while 21.9% showed Nausea, vomiting, headache and constipation. In this study, about half of the participants show intermediate adherence 52.4% The phosphate level was significantly low in high adherence group. Phosphate binders widely used among hemodialysis patients. The phosphate level was affected by the extent of adherence to the phosphate binders where high control level of phosphate was seen in high adherence population. About patients' knowledge towards phosphate binders, most of them reported the right answer toward indication of phosphate binder, while those dealing with dosing, their knowledge was insufficient.

INTRODUCTION

Hyperphosphatemia is an important clinical condition commonly occur among patients with end-stage renal disease (ESRD) It is significantly association with cardiovascular disorders[1] and increases the risk of fractures and osteoporosis in dialysis patients.[2] Hyperphosphatemia may be

effectively managed with phosphatebinder medication therapy, dietary restriction, and dialysis prescription.[3] Phosphate binder medication therapy is the cornerstone of therapeutic management in hyperphosphatemia[4], and it has been associated with survival benefits. Optimization of phosphate binder use by patients with ESRD to achieve target serum phosphorus levels toward the normal range of 3.5-5.5 mg/dL is of most importance to minimize morbidity and mortality risks. [7, 8]

However, it is estimated that up to 74% of ESRD patients are noncompliant to phosphate binder medication therapy [9, 10].Challenges to adherence include;

Medication- related factors such as high pill counts, complex adjustable schedules, adverse side effects, and financial burden [11]

Patient-specific factors such as limited knowledge about the importance of taking binder medications [11, 12]

Recurrent hospitalizations disrupting the usual daily approaches to binder medications, and concomitant comorbidities such as diabetes and hypertension compounding medication complexity and overall burden [12].

Provider-level factors related to educational and emotional support for patients [11].

“High dietary phosphorus intake and increased dietary phosphorus-to-protein ratio have been associated with mortality in ESRD [11]." A low-phosphorus diet is insufficient to control the serum phosphorus level in the well-nourished ESRD patient, and has not been associated with improved survival." Dietary phosphorus restriction is complex because it is challenging to maintain the adequate protein intake needed in ESRD patients to prevent malnutrition and simultaneously restrict phosphorus intake. Perhaps even more importantly, many processed foods contain a significant amount of phosphate additives that are often undisclosed and difficult for patients to identify [11].

“In ESRD, the ideal daily phosphorus intake is 700 mg/day; however, the usual intake commonly averages 1,000-2,000 mg/day." Approximately 60% of the phosphorus is absorbed [12]," which results in a significant daily excess of phosphorus. Adherence to a low- phosphorus diet could be as low as 43% [13], and is influenced similarly by; -

1- diet-specific factors such as menu selections, impact of the diet on social outings, and acceptance of the diet by friends and family [13]; 2- patient factors such as depression, limited self-efficacy, and poor coping skills; and 3- provider factors including inadequate support, infrequent contact with dietitians, and conflicting phosphorus diet advice from different health professionals[14].

"Thrice-weekly conventional dialysis removes phosphorus in the range of 1,800-3,600 mg and, thus, does not provide enough clearance of the daily amount of ingested phosphorus to maintain balance. [15].

Dialysis treatments are complicated by non-adherence, and it is estimated that up to 35% of patients miss treatments entirely whereas another 32% shorten their treatment time [16]. Reasons for non-adherence to the prescribed dose of dialysis include treatment- and patient-related factors. Dialysis vintage and schedule assignment, both, are associated with treatment non-adherence [17]."

Patient factors associated with dialysis treatment non-adherence include younger age [17,18] and non-white race[19] as well as psychosocial factors including negatively perceived effects of kidney disease on daily life and lack of perceived control over future health." Non adherence to the dialysis procedure contributes to significant morbidity and increases mortality risk-in part, due to uncontrolled mineral bone disease [20]. There are unique drivers of adherence behaviours for medications, diet, and dialysis in the effort to control phosphorus, but there are also common themes that can be leveraged to simultaneously optimize all approaches [21, 22].

Aim of the Research

The aim of this study was to assess adherence and knowledge toward phosphate binders in chronic dialysis patients in Karbala and to further investigate if any of patient demographic characteristics or biological variables affect phosphate binder adherence.

RESEARCH METHOD

A cross-sectional study, descriptive, single arm study was done to evaluate the patient's adherence and knowledge toward phosphate binder medications in chronic hemodialysis patients with hyperphosphatemia. The study was conducted at the hemodialysis center in Al-imam Al-Hussein Hospital in Karbala throughout October to December 2022. Chronic dialysis patients using phosphate binders received oral information about the study. Inclusion criteria were: 1) age > 18 years, 2) on maintenance chronic dialysis two to three times a week for at least 6 months, 3) life expectancy > 6 months, 4) using at least one self-administered phosphate binder, 5) able to speak, read Arabic language and 6) able to give oral informed consent. Demographic data were collected from the medical record and by face-to-face interview. In the study, the serum phosphate levels were also collected from the medical records for included patients. The collection of the data was done once time during the research. All eligible participants were asked to answer two questionnaires [Patient Knowledge questionnaire and Morisky Medication Adherence Scale].

The adherence of participants to their phosphate binder was evaluated by applying Morisky questionnaire. All participants were responded to the questions.
Arabic version was obtained of Morisky questionnaire by expert panel from al-Safwa College - department of pharmacy. As seen the in figure (1). The closed- ended questions is pattern of the questionnaire, therefore, the participants were responded by either Yes or No. The Morisky Scale is simple tool used to help identify barriers to medication adherence. The tool can help healthcare providers detect/predict patient behavior and appropriately tailor patient education and treatment strategies.
Interpretation/Scoring: Score 1 point for every YES answer:

0 points = high adherence
1-2 points = intermediate
3-4 points = low adherence

Morisky Scale has proved to be a valuable resource to address adherence concerns, such as; forgetting to take medications, discontinuing medications without guidance either when felt better or worse and neglecting about taking their drug. If patient scores lower on the scale, they are evaluated as more adherent. If they score higher on the scale, they are presumed to be struggling with non-adherence. By understanding how the patient scored on the scale, clinicians and health organizations can identify underlying issues that prevent patients from taking their medications correctly.

The knowledge of participants regarding their phosphate binder was evaluated by applying [Patient Knowledge questionnaire]. all participants were responded to the questions. Arabic version was obtained of Patient Knowledge questionnaire by expert panel from al-Safwa college - department of pharmacy. Patient Knowledge was assessed by a six-item multiple-choice questionnaire based on the questionnaire developed by Eide et al, as outline in (Fig. 2).

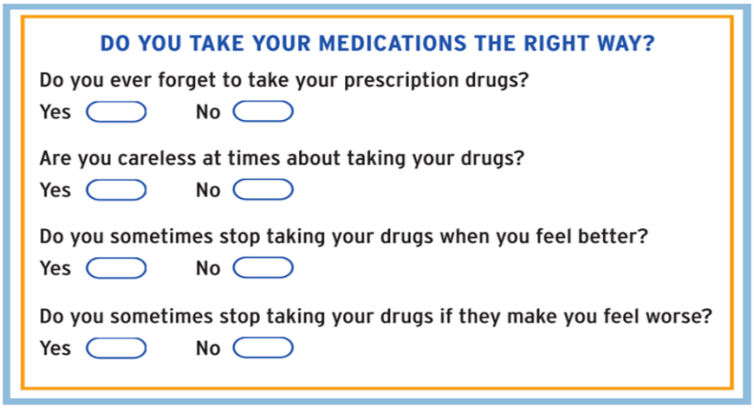

Figure 1: MORSKY score

Questionnaire <<Knowledge regarding phosphate binders>> Mark the answers you find to be correct. There may be several answers to one question. The questionnaire has one pages with a total of six questions.

1. For what condition do you receive phosphate binder?

a- High blood pressure

b- Diabetes

c- High serum phosphate

d- Low serum phosphate

e- I do not know

2. What would you want to prevent by using phosphate binders?

a- Itches of the skin

b- Red eyes

c- Development of diabetes

d- Heart attack

e- I do not know

3. When should you take your phosphate binder?

a- In The evening

b- In The morning

c- For each meal

d- It dose not matter

e- I do not know

4. What might be symptoms of side effects of the phosphate binders?

a- Nausea

b- Vomiting

c- Constipation

d- Head ache

e- I do not know

5.What should you do if you have forgotten to take your phosphate binder?

a- Take double dose with the next meal

b- Take the next dose as normal with a meal

c- It does not matter if you forget a dose

d- I do not know

e- Take half dose at with the next meal

6. Which of these foods/beverages contains a lot of phosphate?

a. Milk

b. Cola

c. Water

d. Jam

e. Honey

Figure 2: Questionnaire (Knowledge regarding phosphate binders)

DATA ANALYSIS

204 patients were included in the study where all participants were asked about adherence and knowledge to their treatment (phosphate binders). In the current study (50-60) years represent the

ages of most participants by 27.9 %, while those with less than 20 years and above 70 years, represent the lowest Ages by 1% and 4.4 % respectively. Furthermore, (60-70), (40-50), (30-40), (20-30) years are the ages of other Participants by 24%, 17.29%, 19.1%, 6.4% respectively as shown in Figure (2). Additionally, mean age of patients was (49.85 ± 13.93) with maximum age was 85 years and minimum age was 18 years.

According to the gender distribution, the males were represented the most of participants by (N=129, 63.2%), while female were represented by (N=75, 36.8%) of patients, as shown in figure 3. In regard to residence of patients, the percentage of residence from inside of Karbala was 97.5 %, while the percentage from outside of Karbala was 2.5%. In regard to those from Karbala governorate, their distribution was9.8% from the Towaireej city, followed by Al-Amel district by 7.8%, Al-Hussainia city by 6.9%, Al-Abbasia city by 6.4%, Al-Hurr by5.4%, SaifSaad, Al-Muwadhafin, Al-Askari and Al-Ghadeer by 2.9%.

Regarding to distribution of patients according to cause of chronic renal disease, the study shows the major cause of chronic kidney disease in most patient was hypertension with percentage (N=70, 34.3%), followed by diabetes mellitus by 15.7%, blood pressure and diabetes by 10.8%, drug induce by 4.4%, and kidney stones by 3.9%, While the cause was unknown in 18.1%. As shown in table 1.

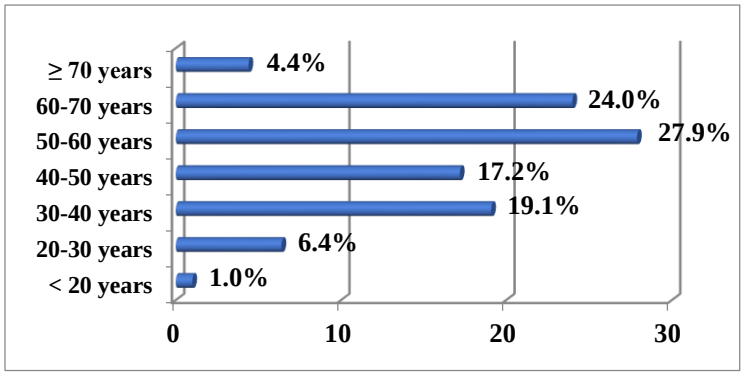

Figure 3: Distribution of patients according to age (N=204)

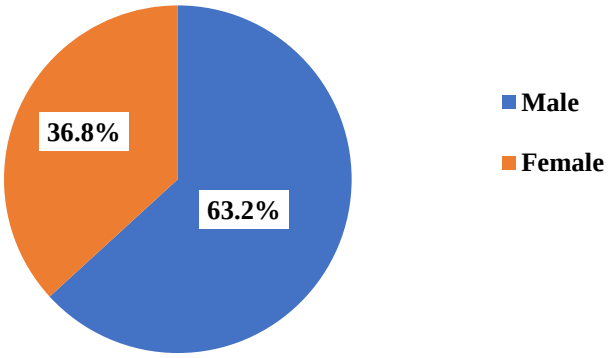

Figure 4: Distribution of patients according to gender (N=204)

Table 1: Distribution of patients according to cause of renal failure (N=204)

cause of renal failure	Frequency	%
Hypertension	70	34.3%
Diabetes mellitus	32	15.7%
Diabetes mellitus and Hypertension	22	10.8%
Renal Stone	8	3.9%
Drug induce	9	4.4%
Heart failure	4	2.0%
Polycystic kidney disease	4	2.0%
Anemia	2	1.0%
Post renal obstruction	1	0.5%
Infection	3	1.5%
Glomerular disease	2	1.0%
Hyperthyroidism	1	0.5%
Nephrotic Syndrome	1	0.5%
Obstructive nephropathy	1	0.5%
Benign prostatic hypertrophy	1	0.5%
Nephrotic Syndrome and COVID-19	1	0.5%
Hypertension and drug induce	1	0.5%
Hypertension and glomerular disease	2	1.0%
Hypertension and Nephrotic syndrome	1	0.5%
kidney stones, hypertension and diabetes mellitus	1	0.5%
Unknown	37	18.1%
Total	204	100.0

In respect to Knowlagent of participants, the questions,' For what condition do you receive phosphate binder?'' and ''What would you want to prevent by using phosphate binders'' that related to use phosphate binder were 58% and 69%, respectively, of participants responded accurately while the others (42%, 31% respectively) did not know the right answer.

In regard to the questions, ''When should you take your phosphate binder?'' and' 'What should you do if you have forgotten to take your phosphate binder?'' that related to dose of phosphate binder, 37.2% and 4.9% respectively of the participants were answered properly while most of the others did not answer accurately (62.8% and 94.1% respectively).

In regard to ''what might be symptoms of side effects of the phosphate binders? '' (20.1%) of participants said they got some nausea by when using (sevelamer). Furthermore, 21.6% of the participants reported vomiting, constipation, headache or nausea with these symptoms. While (58%) did not know, if there are side effects or not! About the question (Which of foods/beverages contains a lot of phosphate), the answers were (23%) cola and (31%) water then honey 12.7% and milk 7.4, while the other answers were reported in table (2)

In relation to Morsky score, the participants were allocated in to three groups as follow, high adherence 21.1%, intermediate adherence 52.4% and low adherence 27.5 % as shown in figure (3). The phosphate level was significantly low in high adherence group (4.62 ± 1.31) when compared to intermediate (5.34 ± 1.61) or low adherence group (5.31 ± 1.55) as shown in table (3) and figure (5). In respect to relationship of demographic data (age, gender), the cause of chronic kidney with adherence, there was insignificant dependent of adherence to these variables as shown in table (3). The Patients with high adherence present with significant mean reduction in serum phosphate level.

Table 2: Distribution of patients according to their answers about the following questions

Questions	Number	%
For what condition do you receive phosphate binder		
High blood pressure	11	5.4%
Diabetes mellitus	1	0.5%
High serum phosphate	120	58.8%
Low serum phosphate	16	7.8%
I do not know	56	27.5%
Total	204	100.0%
What would you want to prevent by using phosphate binders	141	69.0%
Itches of the skin	5	2.5%
Red eyes	3	1.5%
Itches of the skin and red eyes	2	1.0%
Development of diabetes	0	0.0%
Heart attack	53	26.0%
I do not know	204	100.0%
Total		
When should you take your phosphate binder		
In the evening	13	6.4%
In the morning	55	27.0%
In the evening and morning	47	23.0%
For each meal	76	37.2%
It does not matter	8	3.9%
I do not know	5	2.5%
Total	204	100.0%
What might be symptoms of side effects of the phosphate binders	41	20.1%
Nausea	9	4.4%
Vomiting	7	3.4%
Constipation	7	3.4%
Headache	6	2.9%
Nausea and vomiting	4	2.0%
Nausea, vomiting and constipation	2	1.0%
Nausea, vomiting, constipation and headache	2	1.0%
Nausea and constipation	4	2.0%
Nausea and headache	1	0.5%
Vomiting and constipation	1	0.5%
Vomiting, constipation and headache	1	0.5%
Vomiting and headache	119	58.3%
I do not know	204	100.0%
Total		
What should you do if you have forgotten to take your phosphate binder	123	60.3%
Take double dose with the next meal	10	4.9%
Take the next dose as normal with a meal	0	0.0%
Take half dose at with the next meal	1	0.5%
Take double dose with the next meal and take the next dose as normal with a meal	59	28.9%
Dose not matter if you forget a dose	11	5.4%
	204	100.0%

Don't know Total		
Which of these foods/beverages contains a lot of phosphate Water Cola Milk Jam Honey Water and Cola Water, Cola and milk Water and milk Water, Cola, milk and Jam Cola and Jam Cola and milk Total	64 47 15 12 26 16 19 1 1 1 2 204	31.4% 23.0% 7.4% 5.9% 12.7% 7.8% 9.3% 0.5% 0.5% 0.5% 1.0% 100.0%

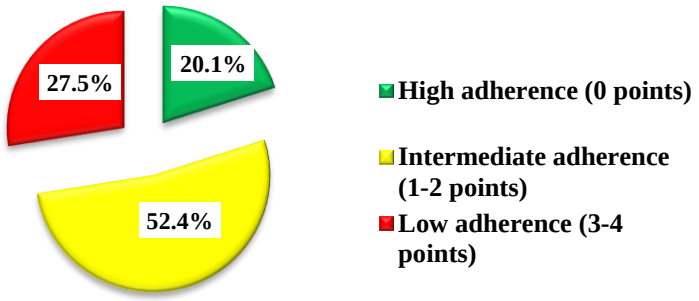

Figure 5: Distribution of patients according to adherence (N=204)

Table 3-A: The mean differences of phosphate (mg/dl) according to adherence

Study variable	Adherence	N	Mean ± SD	F-test	P-value
Phosphate (mg/dl)	High	41	4.62 ± 1.31	3.492	0.032*
	Intermediate	107	5.34 ± 1.61		
	Low	56	5.31 ± 1.55		
	Total	204	5.19 ± 1.56		

Figure 5-B: Multiple comparison (LSD)

Adherence	Adherence	P-value
High adherence	Intermediate	0.011*
	Low	0.031*
Intermediate adherence	High	0.011*
	Low	0.89
Low adherence	High	0.031*
	Intermediate	0.89

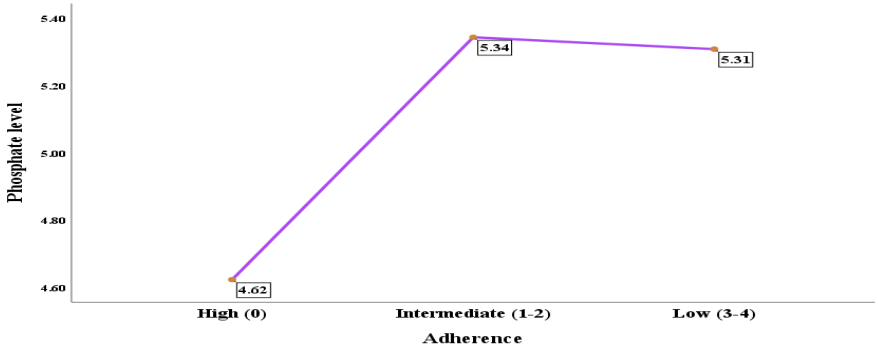

Figure 6: The mean differences of phosphate (mg/dl) according to adherence (P=0.032*)

DISCUSSION

This study shows correlation between increasing in ages and likelihood of has CKD and dialysis in addition, there is a study by: the Public Health Agency of Canada (50) Prove relationship between ages and chronic diseases and disability that cause by it One last thing we can noticed by results, ages above 70th are the most less percents among other, this is may be cause by averages of life of humans. The majority of our participants were males (63%) and females (36%).

Studies show that although more women than men have chronic kidney disease (CKD), men are more likely to reach kidney failure sooner than women. That's why being male is used as a risk factor to predict a faster time to reach kidney failure. The reasons for these gender differences are not clearly understood. Women may be more likely to have CKD because of getting urinary tract infections more often, which can lead to kidney damage. Women also have increased risk for kidney damage due to problems with pregnancy, such as high blood pressure or eclampsia [23]. The incidence of acute kidney injury in patients with pre-eclampsia/eclampsia is high (42.86%). The presence of eclampsia in patients admitted with severe pre-eclampsia is associated with the development of AKI within 48 h after hospitalization. We recommend a larger prospective study that will include the use of biomarkers for acute kidney injury and closer monitoring of mothers with eclampsia for features of acute kidney injury. It is also important to increase both clinician and patient awareness to minimize the risk of AKI in women with pre-eclampsia [24].

Men may be at increased risk of reaching kidney failure sooner than women because of differences in hormone levels. Higher testosterone levels in men may cause a loss in kidney function. On the other hand, men's kidneys may not be protected by estrogen, which is higher in women until menopause, overall, men may have unhealthier lifestyles, thereby leading to a higher risk for kidney failure. And in studies, men may have been counted as having kidney failure at a younger age than women because they may have gotten dialysis or a kidney transplant sooner than women. Although more women may have had kidney failure, they may not have been counted in studies because they weren't on dialysis or didn't have a kidney transplant. It's not always easy to be healthy or have a healthy lifestyle. And why is that? Well—the short answer is that many people, especially people living, working, and learning in under-resourced communities, simply do not have access to the very basics that are needed, such as open and green spaces like parks, reliable public transportation, healthy foods to eat, and appropriate medical care [25].

Residences of dialysis Proportional to two factors: A-Population density, as we can noticed in (amel) and (towerij) which they are known by high births; B-Level of education and income, Poor residents sharing low education and health as usual; C-Risk factors: There are a number of environmental and social factors that can increase your risk of developing kidney disease. These SDoH contribute to

developing serious chronic conditions such as high blood pressure, diabetes (also called sugar diabetes or sugar disease), lupus, or being overweight, which can lead to kidney disease. In addition, your genetics or having family members with kidney disease may also play a role [26].

Patients' deficiency knowledge of phosphate binders, as shown by the fact that less than 40% of correct answer regarding dose phosphate binder (when to take them and what do you do if you oblivion taking the dose of phosphate binders). concerning questions to identifying foods and beverages high in phosphate the answer 31.4% (correct answer). This knowledge difference is important especially for patients with chronic kidney disease who need correct and carefully manage their phosphate intake [27].

The lack of knowledge among patients can be a mind to adherence to phosphate binder, and this can be resulting not good outcomes. Patients are given the sufficient information about the importance of phosphite Binder and how Commitment of give drug and also education patients about adverse effects of phosphate binders and what happens if forgetting the dose [28]. And also monitoring adherence of patients and also healthcare should be Their role is engaged in patients. Developing a collaborative relationship between healthcare and patients is important to control and obtained outcome good and improve Quality of life and also Education is insufficient on communication sites of phosphate binders. However, the percentage of cases that true answer was 58.8%, Comparison with a study that noticed that 80% the mean of patients' Natural condition of phosphate binders where have poor knowledge on dietary phosphate control and also drug phosphate binder. where can point that such as this type adherence can be reflected patients' commitment to treatment with phosphate binder, which was not built on knowledge depend on phosphate dietary control and What can influence the effectiveness of phosphate Binder.

According to MORSKY score, most of participants were present with intermediate (52.4%), while the remaining were present either with high adherence (27.5%) or low adherence (20.1 %). Overall mean score of MORSKY was 1.65 that could interpreter as intermittent adherence. These finding could be correlate with level of knowledge that reported in the current study, especially question that related to dose of phosphate binder where only 37.5% responded appropriately. Furthermore, the current results were also could be correlate with level of phosphate, lower phosphate level was observed in high adherence population, which considered significantly lower level than those with intermittent or low adherence whose have higher phosphate level.

Medications adherence is known to be determined by factors related to the patient, medication/disease, socioeconomic status, the healthcare system, etc. [29-32]. In our study the adherence was affected by (age and gender). By age group, adherence in the 18-30 group was the lowest with 7.4%, and it gradually increased as the age increased with the adherence being at 17.2% and 27.9% in the 40 to 49 and 50 to 59 age group, respectively. Adherence peaked at 60 to 69 age group with 28.4 %. Some other studies also reported that medication adherence increases with age [33-36]. The reason for this tendency is that older patients generally have greater severity of illness than younger ones, which increases their awareness about their health status, and this seems to have a positive effect on adherence [37].

While in regard to sex, this study appeared insignificant differ among adherence population. Evidence on the relationship between gender and adherence is mixed, with some studies suggesting that female patients have a higher level of adherence [38], others that males have a higher level of adherence [39] and others that there is no relationship between gender and adherence [40].

The most common cause of low adherence among dialysis patients were established from; adverse effect, forgetfulness, cost, and most of patient of CKD were presented poly pharmacy [41]. In our study, the reasons of low adherence may be related to; low level of knowledge, unavailability of phosphate binder in center, adverse effect that mostly nausea, high cost in private sector. Other study

found a consistent inverse relationship between cost-sharing and worse adherence. Higher cost-sharing was consistently associated with lower adherence to prescribed medication [42-44].

FINDINGS AND RECOMMENDATIONS

Phosphate binders' usage is frequent among hemodialysis patients in Al-Hussein center. The phosphate level was affected by the extent of adherence to the usage of phosphate binders where mean score of Morsky is (1.65± 1.15) that interpreted as intermediate adherence. Furthermore, low level of phosphate was seen in high adherence population.

In regard to the patients' knowledge towards phosphate binders might be important for patients' motivation for being adherent. Furthermore, the questions that related to indication of phosphate binder, most of participants were responded the appropriate answer. While those dealing with dosing, their response was not appropriate.

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