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ORIGINAL ARTICLE

Anxiety and Depression among Hemodialysis Patients in Egypt

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ABSTRACT

Background: Anxiety and depression are frequently found in hemodialysis (HD) patients. They remain understudied and often untreated that increases the suffering of such patients.

Methods: We studied the prevalence, demographic, clinical and laboratory predictors of anxiety and depression among 524 HD patients in Sharkia Governorate, using the Hospital Anxiety and Depression Scale (HADS) Questionnaire.

Results: 51% and 33.7% of patients had borderline and abnormal anxiety scales respectively, while 52.3% and 31.9% had borderline and abnormal depression scales respectively. 34.2% and 48.6% of patients with borderline and abnormal anxiety scales had hypertension respectively, while 24.1% and 21.5% of patients with borderline and abnormal anxiety scales had diabetes mellitus (DM) respectively. Married patients represented 81.9% and 82.5% of patients with borderline and abnormal anxiety scales respectively. Anxiety had a negative correlation with HD duration and a positive correlation with alkaline phosphatase (ALP) levels, while depression had a positive correlation with both ALP and C-reactive protein (CRP) levels. CRP presented more in patients with borderline and abnormal depression scales (25.9% and 19.9% respectively).

Conclusions: Anxiety and depression are common in Egyptian HD patients. Anxiety has a negative correlation with HD duration and a positive correlation with ALP. Depression is common in patients with DM and hypertension. It has a positive correlation with ALP and CRP levels. Also, married patients and those with high CRP levels are more prone to have depression.

Keywords: Anxiety; Depression; Hemodialysis (HD), Hospital Anxiety and Depression Scale (HADS) Questionnaire

INTRODUCTION

End-stage renal disease patients (ESRD) are increasing in number worldwide every year, and in parallel; the number of hemodialysis (HD) patients is increasing as well [1]. The impact of HD therapy is expensive, invasive, and timeconsuming that requires multidisciplinary and comprehensive care for the patients as well as their families. This set of factors adversely affects the lives of patients, both physically and psychologically [2].

Psychiatric illnesses in patients with ESRD has persistently intrigued healthcare workers due to its effect on the morbidity and healthcare costs in patients with ESRD. The term psycho-nephrology refers to psychiatric problems of people suffering from kidney disease, particularly those with kidney failure who undergo maintenance dialysis or transplantation [3].

Anxiety and depression are the primary psychiatric problems of ESRD patients with an estimated prevalence of about 3 times that of the general population [4, 5]. The National Institute of Mental Health defines anxiety disorder as an excessive, irrational dread of everyday situations. Uremic and depressive symptoms overlap considerably, and it is sometimes difficult to define depression in ESRD [6].

However, clinical depression is a medical condition associated with significant subjective suffering, impairment of social and occupational functioning and lower health-related quality of life (QOL) [7]. Anxiety and depression disorders are independent risk factors for suicidal behavior, morbidity, poor QOL, disability and mortality [8, 9, 10].

The Hospital Anxiety and Depression Scale (HADS) Questionnaire was used to screen for anxiety and depression. It is of great importance to diagnose anxiety and depression in medical patients, and the HADS selfassessment scale is intended to help clinicians to obtain an early indication for possible psychiatric disorder symptoms which might improve with treatment. The HADS has been reported to be an effective screening tool in several medical settings [11,12].

To our knowledge, this is the first study to use HADS Questionnaire to screen anxiety and depression in Egyptian HD patients (Sharkia governorate). The goal of this study was to screen the prevalence and predictors of depression and anxiety in those group of patients.

METHODS

Study Design and Populations:

This is a cross-sectional study, carried out in HD units of Sharkia governorate which locates in the East of the Egypt-Delta from December 2018 to March 2020.

Ethical Approvals:

We got the approvals from the local Institutional Ethics Committee and conformed to the Helsinki Declaration. we explained the aim of the study to the included patients. Informed and written consent had been taken to participate in the study.

Population of the Study:

Demographic information was collected; The total number of the study was 612 HD patients, 88 were excluded due to withdrawal, refusal and/or incomplete data. Thus, the enrolled final number became 524 HD patients, among them 288 males (53.1%) and 236 females (46.9%), with a mean age of 51.95 ± 13.51 years (range from 19 to 70 years). The main causes of ESRD in our studied group of patients were chronic glomerulonephritis (32.1%), diabetic nephropathy (21.4%), interstitial nephropathies (15%), obstructive uropathy (6.4%) and unknown (25.1%).

Inclusion Criteria:

Eligible participants included adults with stable clinical condition on regular HD, with good verbal agreement to the questionnaire, hemodialysis was for at least 6 months before the study, and the mean period of dialysis was 30.5 ± 27.66 months (range from 6 - 240 months). Dialysis was performed three times per week, 4 hours each, using polysulfone membranes and 3 mEq/l dialysate calcium, protocols were not changed during the study with adequate dialysis treatment (Kt/V>1.2), follow-up visits were conducted at the dialysis centers within 12 months after enrollment.

Exclusion Criteria:

Participants were excluded from the study if suffering from major visual or hearing impairments, severe cerebral vascular disease, chronic liver disease, major heart, lung diseases or malignancies that can add additional psychological burden other than HD.

Laboratory Investigations:

The results of the most recent routine laboratory testing (within 1 month) were recorded, including complete blood count (CBC), renal and liver function tests, C-reactive protein (CRP) (mg/L), serum Albumin (mg/dL), intact parathormone (iPTH) (pg/mL), corrected serum calcium (Ca) (mg/dL) and serum phosphorus (mg/dL). Samples were centrifuged, quoted, and stored at -80 C and were transported to the laboratory. We measured serum albumin, and CRP in duplicate on each serum sample using a Beckman Array 360 nephelometer, and the mean values were used in analyses.

The Hospital Anxiety and Depression Scale (HADS) Questionnaire:

The included patients were interviewed face-to-face by the research team. All researchers received practical training on using the HADS to maintain consistency in questionnaire administration. The questionnaire was professionally translated into Arabic.

The HADS was developed by Zigmond & Snaith. The questionnaire was designed to provide a reliable tool within the clinical practice, and it is composed of fourteen items. The scale measures both anxiety and depression on two separate subscales, each containing 7 items. More specifically, items of the HADS are scored from 0 to 3 on a Likert Scale with a final score ranging from 0 to 21 for either anxiety or depression. For each subscale, participants were grouped as normal (0–7 of 21), borderline abnormal (8–10) and abnormal (11–21) [13]. *Statistical Analysis:*

Data were tested using Kolmogorov-Smirnov test for normality and if necessary, logarithmic transformations were used for analysis. Continuous variables were expressed as mean \pm standard deviation and categorical values were expressed in percentages. The differences between the two groups were analyzed using independent sample t-test, and Chi-Square analysis was used for categorical data. Pearson correlations were used to determine the possible correlation between various variables and dependent variables. Statistical significance was defined as P < 0.05. All analyses were performed using the statistical package for the social sciences, version 21.0 for windows (SPSS Inc., Chicago, USA).

RESULTS

A total number of 524 patients participated in the study including 288 males (55%) and 236 females (45%). The mean age of the studied cases was about 60 years (range from 19-70 years), of which 25.6 % were smokers. More than half of the cases were not working (61.3%), of low educational level (59.2%) and 34.4% had financial problems. The mean duration of HD was 30.5 ± 27.66 months (range

from 6-240 months). 40.6% of the cases suffered from hypertension, while 21.6% had DM. 22 patients (4%) had psychiatric illness before the start of HD and 133 patients (25.4%) had major family problems. Most of the cases had family support (76.5%). Hemoglobin (Hb) concentration ranged from 6.8-13.3 gm/dL. Mean serum Ca was 8.57 mg/dl. Mean serum albumin was 4.74 gm/dl. The mean serum ALP was 69.71 IU/L, mean serum cholesterol was 208.45 mg/dl, while mean serum ferritin was 858.17 ng/ml. CRP was positive in 114 patients. (Tables 1 and 2).

More than half of the patients were borderline as regards anxiety and depression scale (51% and 52.3% respectively), while 33.7% and 31.9% of the patients were abnormal cases of anxiety and depression respectively (Table 3).

On correlation study, we found a highly statistically significant negative correlation between anxiety scale and HD duration (p = 0.001), and a significant positive correlation with serum ALP level (p = 0.04). While there was a highly significant positive correlation between depression scale and Serum ALP level (p = 0.001). There was also a significant positive correlation between CRP level and depression scale (p = 0.03) (Table 4).

Most of the studied cases with borderline and abnormal anxiety scale had chronic illnesses, namely hypertension and DM (34.2% and 24.1% in borderline cases and 48.6% and 21.5% in abnormal cases respectively, p = 0.005) (Table 5).

Regarding depression, there was a statistically significant difference among normal, borderline, and abnormal depression scales in married patients (80.7% and 82.5% in borderline and abnormal depression patients respectively, (p = 0.04). The study showed also that positive CRP presented more among borderline and abnormal depression patients (25.9% and 19.9% respectively, (p = 0.01) (Table 6).

	Variables	Number	Percentage (%)
Gender	Male	288	55
	Female	236	45
Age	<20 years	39	7.4
	20–40 years	179	34.2
	>40 years	306	58.4
Marital status	Single	36	6.9
	Married	427	81.5
	Divorced or separated	10	1.9
	Widower	51	9.7
Number of children	No children	53	10.1
	1-4	403	77
	5 or more	68	12.9
Educational level	Unenlightened	310	59.2
	Secondary school or less	181	34.5
	Parchment	33	6.3
Work status	Yes	203	38.7
	No	233	44.5
	Retired	88	16.8
Smoking	Yes	134	25.6
	No	390	74.4
Financial problems	Yes	180	34.4
	No	344	65.6
Residence	City	174	33.2
	Village	350	66.8
Duration of renal failure (years):	<1	118	22.5
	1-5	283	54
	>5	123	23.4
Chronic illness:	Hypertension	213	40.6
	DM	113	21.6
	IHD	11	2.1
	SLE	12	2.3
	Others	174	33.2
Psychiatric illness before HD:	-	21	4
Restless leg syndrome:	-	48	9.2
Major family problems	-	133	25.4
Family support:	-	401	76.5
HD duration in months (mean±SD)	30.5 ± 27.66 (range from 6-2	240 months)	
BMI (mean±SD)	24.3±18		
MAP in mmHg (mean±SD)	97.5±14.42		

Table (2): Laboratory data of the studied population.

Variable	Mean \pm SD (N=524)	Minimum	Maximum
Hb (gm/dl)	11.3±40.76	6.8	13.3
iPTH (pg/mL)	384.9±410.45	7	3502
Serum Calcium (mg/dl)	8.57±3.77	5.2	88.8

Variable	Mean \pm SD (N=524)	Minimum	Maximum
Serum Phosphorus (mg/dl)	5.21±2.62	2	42.6
Calcium × Phosphorus	42.1±11.29	5.6	92.3
Serum ALP (IU/L)	69.71±73.18	4	1333
Serum albumin (gm/dL)	4.74±12.69	2.3	210
Serum total Cholesterol (mg/dL)	208.45±26.26	20	320
Serum ferritin (ng/mL)	858.17±674.7	25	2962
CRP (mg/L) < 10 (negative)	410	0.7	9.6
> 10 (positive)	114	10.3	18.9

Hb: Haemoglobin, iPTH: intact parathormone, ALP: alkaline phosphatase, CRP: C-reactive protein. **Table (3):** Prevalence of anxiety and depression among the studied population.

Variable	Anxiety scale		Depression	n scale
	Ν	%	Ν	%
Normal cases	80	15.3	83	15.8
Borderline cases	267	51	274	52.3
Abnormal cases	177	33.7	166	31.9

Table (4): Correlation between anxiety and depression with laboratory and clinical data of the studied population.

	Anxiety scale		Depression scal	e
	R	P value	R	P value
HD duration	-0.155	0.001	0.006	0.901
MAP	0.291	0.231	-0.250	0.167
BMI	0.098	0.976	0.007	0.112
Hb %	-0.398	0.345	-0.174	0.234
Serum iPTH	-0.334	0.632	-0.212	0.324
Serum calcium	-0.665	0.234	-0.406	0.232
Phosphorus	-0.189	0.110	0.238	0.112
Calcium×Phosphorus	-0.145	0.986	-0.216	0.654
Serum ALP	0.435	0.04*	0.551	0.001*
Serum albumin	0.172	0.543	0.09	0.342
Serum total cholesterol	0.231	0.222	0.324	0.117
Serum ferritin	0.041	0.754	0.222	0.745
Serum CRP	0.215	0.108	0.632	0.03*

MAP: mean arterial pressure, BMI: body mass index, iPTH: intact parathormone ALP: alkaline phosphatase.

Table (5): Relation between demographic and clinical data of studied population and anxiety scale:

Variable	Normal (N=80)		Borderline (N=267)		Abnormal (N=177)		Chi- Square	P-value
	Ν	%	Ν	%	Ν	%		
Gender								
Male (n=288)	46	58.2	150	56.2	92	52	1.14	0.567
Female (n=236)	34	41.8	117	43.8	85	48		
Smoking								
Yes (n=134)	16	20	76	28.5	42	23.7	2.66	0.265
No (n=390)	64	80	191	71.5	135	76.3		

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Variable	Normal			Borderline		Abnormal		P-value
	(N=80) N	%	(N=267) N	%	(N=177) N	%	Square	
Work state		70		70		70		
Worker (n=203)	32	40	108	40.1	63	35.6	9.22	0.162
Not work (n=321)	48	60	159	59.9	114	64.4		
Educational level								
Low level (n=310)	45	56.3	159	59.6	106	59.9		
Average (n=181)	31	38.7	85	31.8	65	36.7	6.33	0.176
High (n=33)	4	5	23	8.6	6	3.4		
Marital state								
Married (n=427)	68	84.8	220	82.4	139	78.5		
Divorced (n=10)	0	0.0	5	1.9	5	2.8	6.24	0.345
Widow (n=51)	4	5.1	27	10.1	20	11.3		
Single (n=33)	8	10.1	15	5.6	13	7.3		
Financial problems								
Yes (n=180)	22	27.5	105	39.3	53	29.9	5.93	0.05
No (n=344	58	72.5	162	60.7	124	70.1		
Family problems								
Yes (n=133)	19	24.1	66	24.7	48	27.1	0.417	0.812
No (n=391)	61	75.9	201	75.3	129	72.9		
Chronic illness	26	15 6	01	24.2	0.6	10 6		
HTN (n=213)	36	45.6	91	34.2	86	48.6		
DM (n=113) CHD (n=11)	11	13.9	64 10	24.1 3.8	38	21.5	21.8	0.005*
SLE (n=12)	0 0	0.0 0.0	8	3.8 3	1 4	0.6 2.3	21.0	0.003*
Others $(n=174)$	32	40.5	8 93	35	4	2.3		
Restless leg syndrome	52	-0.5	15	55	-0	27.1		
Yes (n=48)	8	10.1	21	7.9	19	10.7	1.15	0.56
No (n=476)	71	89.9	246	92.1	158	89.3	1.15	0.50
Psychiatric illness	/ 1	0717	- 10	/=	100	0710		
Yes (n=21)	6	7.6	7	2.6	7	4	4.11	o.128
No (n=503)	73	92.4	260	97.4	170	96		
Family support								
Yes (n=401)	62	77.2	201	75.3	138	78		
No (n=123)	18	22.8	66	24.7	39	22	0.45	0.797
CRP								
Positive (n=114)	15	17.7	58	21.7	41	23.2	0.96	0.619
Negative (n=410)	65	82.3	209	78.3	136	76.8		

Table (6): Relation between demographic and clinical data of studied population and depression scale:

	Normal N=83		Borderline N=275		Abnormal N=166		Chi-sq	P-value
Variable	Ν	%	Ν	%	Ν	%		
Gender Male (n=288) Female (n=236)	47 36	56.6 43.4	151 124	54.9 45.1	90 76	54.2 45.8	0.13	0.937
Smoking Yes (n=134) No (n=390)	22 61	26.5 73.5	73 202	26.6 73.4	39 127	23.5 76.5	0.578	0.749

	Normal N=83		Borderline N=275		Abnormal N=166		Chi-sq	P-value
Variable	N	%	Ν	%	Ν	%	·	
Work state Worker (n=203) Not work (n=321)	39 44	53 47	100 175	36.4 63.6	64 102	38.6 61.4	12.24	0.05
Educational level Low level (n=310) Average (n=181) High (n=33)	47 27 9	56.3 38.7 5	167 93 15	59.6 31.8 8.6	96 61 9	59.9 36.7 3.4	3.81	0.433
Marital state Married (n=427) Divorced (n=10) Widow (n=51) Single (n=33)	68 0 8 7	81.9 0 9.6 8.4	222 2 30 21	80.7 0.7 10.9 7.7	137 8 13 8	82.5 4.8 7.8 4.8	13.57	0.04*
Financial problems Yes (n=180) No (n=344)	27 56	32.5 67.5	93 182	33.9 66.1	60 106	36.1 63.9	0.378	0.828
Family problems Yes (n=133) No (n=391)	14 69	16.9 83.1	68 207	24.8 75.2	51 115	30.7 69.3	5.72	0.06
Chronic illness HP (n=213) DM (n=113) CHD (n=11) SLE (n=12) Others (n=174)	37 14 3 1 28	44.6 16.9 3.6 1.2 33.7	104 63 5 9 93	38.1 23.1 1.8 3.3 33.7	72 36 3 2 53	43.4 21.7 1.8 1.2 31.9	5.83	0.666
Restless leg syndrome Yes (n=48) No (n=476)	9 74	10.8 89.2	25 250	9.1 90.9	14 152	8.4 91.6	0.327	0.824
Psychiatric illness Yes (n=21) No (n=503)	3 80	3.6 96.4	9 266	3.3 96.7	9 157	5.4 94.6	1.77	0.412
Family support Yes (n=401) No (n=123)	69 14	83.1 22.8	215 60	78.2 21.8	117 49	70.5 29.5	5.76	0.06
CRP Positive (n=114) Negative (n=410)	9 74	10.8 89.2	72 203	25.9 74.1	33 133	19.9 80.1	8.96	0.01*

DISCUSSION

This study aimed to determine the prevalence of anxiety and depression among HD patients in Sharkia governorate, Egypt and to assess any possible association between those two conditions and different demographic, clinical and laboratory parameters. We noticed that anxiety and depression were highly prevalent among HD patients with a prevalence rate of 51% and 33.7% for borderline and abnormal anxiety cases respectively, and 52.3% and 31.9% for borderline and 31.9% for abnormal depression cases respectively. These results are lower than that was reported in a study done in Malaysia where they found ,157 patient (71.3%) had depression at baseline, and169 (78.2%) had depression on 2nd evaluation and 181 (84.9%) on the final visit [13]. However, previous studies reported a comparatively similar rates of depression among HD patients, ranging from 23.3 to 60.5% [14, 15, 16].

A recent review and meta-analysis by Palmer et al. They checked the prevalence of depression in HD populations [17]. They identified 216 studies of 55,982 patients with CKD or ESRD. Among patients with ESRD receiving dialysis, the prevalence of depression was 39.3% when evaluated by screening questionnaires, and 22.8% when evaluated by clinical interview. In patients with CKD, the prevalence of depression was 26.5% when evaluated by screening questionnaires, and 21.4% when evaluated by clinical interview. Prevalence rates were higher in ESRD than in CKD when questionnaires were used to diagnose depression (39.3% vs. 26.5%) but were similar when depression was diagnosed by clinical interview (22.8% vs. 21.4%). This difference is likely related to uremic symptoms (fatigue, insomnia, poor appetite) in ESRD populations that could overlap with somatic symptoms of depression when measured using questionnaires [18].

However, the study done by Fischer et al., reported a prevalence of depressive symptoms of 27.4% using a Beck's Depression Inventory (BDI), a cutoff of 11 among 3853 individuals with mild-to-moderate CKD enrolled in the Chronic Renal Insufficiency Cohort (CRIC) and Hispanic CRIC (HCRIC) studies [19]. This higher prevalence of anxiety/depression in our study may be related to different socioeconomic conditions in different countries. Nevertheless, it was reported that only one-third of the HD patients with a diagnosis of depression were receiving treatment [20].

In the current study, there was a significant negative correlation between anxiety

and HD duration. Anxiety in HD may be related to procedural aspects of dialysis such as, transportation issues, spending considerable time in dialysis units, and the prolonged sitting time during dialysis. Furthermore, patients may suffer adverse outcomes that may trigger distress. Anxiety may also be related to fear of access complications, dialysis-related symptoms, and side effects, which are common concerns among patients on HD [21].

Kimmel et al., identified the same pattern, observing an initial increase in anxiety, which decreased later, probably as patients adapted to the treatment regime [22]. In the current study, most of the studied cases with borderline and abnormal anxiety scale had chronic illnesses, namely hypertension or diabetes. Indeed, the risk of depression and anxiety in patients with CKD had been described to be associated with various clinical parameters.

Comorbidities may increase the risk of development of anxiety and depression. For instance, patients with depressive symptoms were found to have other comorbid illnesses such as hypertension, DM, cardiovascular diseases, hypoalbuminemia, and substance abuse [23, 24]. Similarly, an analysis of 628 black individuals with CKD and HTN from the African American Study of Kidney Disease and Hypertension (AASK) cohort found a 42% depression prevalence which is much higher than that observed in other mixed race/ethnicity CKD populations [25].

The underlying reasons for this finding could be the lifelong diseases that added an additional burden on the dialysis procedures 3times per week, patients taking too much medicine at once, economic burden on patients and their families and altered family and social relationships. On the other hand, Lopez et al. revealed that patients with DM (without independently hypertension) were and significantly associated with a higher likelihood of self-reported depression as measured by the "so down in the dumps" question [26]. This difference in this association could be explained using different scales to diagnose depression, different socio-economic circumstances, and different logistics of dialysis services in different countries.

We found also that in patients with borderline depression, 222 patients out of 275 (80.7%) were married while, in those with abnormal depression scale, 137 patients out of 166 (82.5%) were married. Those results are in the same way of Amjad et al., they found that 165 (84.6%) out of 195 married patients, were having depression in their study [13]. In contradiction to our findings, other studies reported that depression was less common in married people on dialysis therapy while divorced/widowed patients were at higher risk of depression [27].

Also, in a study done in Taiwan, marriage in HD patients was significantly associated with better quality of life [28]. Additionally, Kimmel et al., reported that the rate of depression was higher among divorced and widowed women [29]. It is postulated that supportive and peaceful family environment, happy married life and family support is associated with less anxiety/depression and better quality of life in chronic HD patients [30].

For unknown reason, it seems that this was not the case in our study. The current study showed a positive correlation between ALP level and both anxiety and depression. Serum ALP commonly includes isoenzymes from bones, liver, intestine, leucocytes, and kidneys [31]. The osteoblast is the prominent source of ALP. As hyperparathyroidism and high-turnover bone disease are common in dialysis patients, an elevated ALP level is usually considered as a marker of bone disease and renal osteodystrophy [32, 33] with increased risk of cardiac failure, diastolic dysfunction [34], and cardiovascular disease [35]. Furthermore, Kalantar-Zadeh et al. demonstrated an increased risk of all-cause morbidity and mortality associated with higher ALP levels in HD patients [36].

Nevertheless, few studies assessed the relation between bone mineral metabolism and

anxiety. Najafi et al. found that anxiety was inversely associated with iPTH levels [37]. Part of these differences could be due to differences in patients' metabolism, body structure, nutritional and environmental conditions, activities and severity of depression or anxiety.

In addition, there is a proposed link between ALP and CRP levels in CKD patients, Damera et al. found a positive correlation between ALP and CRP levels independent of serum 25-OH vitamin D in the chronic and non-CKD populations. Hence, serum alkaline phosphatase might be a marker of the inflammatory milieu, like CRP [38]. There is growing evidence also that CRP (a marker of systemic inflammation produced by the liver) is dysregulated and can predict cardiovascular death in ESRD patients [39].

Our study showed a positive correlation between CRP levels and the occurrence of depression. Studies investigating a link between CRP and depression have been mixed, with some studies reporting positive association [40, 41] whereas others found no association [42, 43]. In their study, Valjbona et al. found a positive correlation between serum CRP level and the occurrence of depression, and more than 50% of those patients died from cardiovascular diseases [44]. Other studies found a relationship between depression and inflammatory as well as immune responses [45]. There is a need for larger scale studies to investigate other confounding factors that might play a role in the development of depression in this vulnerable group of patients.

CONCLUSIONS

We can conclude that anxiety and depression are frequent problems in hemodialysis patients but remain underestimated, they are especially commoner in diabetics and hypertensives and married patients. We found that they are positively corelated with ALP and CRP levels, we advise larger scale studies in almost all dialysis centers in Egypt and try to search for other possible diagnostic markers to treat early.

Conflicts of Interest: Nothing to declare.

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