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Gender-Related Differences and Mortality Predictors among Egyptian Hemodialysis Patients: A Multi-Center Prospective Observational Study

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Authors' contributions

This work was carried out in collaboration among all authors. Author AFM gave research idea, performed study design and data acquisition. Author MMTA performed data analysis/interpretation. Author GEK provided intellectual content of critical importance to the work described and author NSA supervised the study. All authors read and approved the final manuscript.

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ABSTRACT

Background: End-stage renal disease (ESRD) is an important cause of global morbidity and mortality affecting both sexes. Both genders may present with different symptoms and signs, respond differently to therapy and may exhibit different degrees of tolerance towards their disease. In Egypt, hemodialysis (HD) constitutes the most common modality of renal replacement therapy and the number of hemodialysis patients is increasing. The objective of the present study was to investigate gender-related differences in clinical and biochemical characteristics in HD patients. Mortality events in both genders were also recorded and predictors of mortality in the included HD population were explored.
Methods: This multicenter study adopted essentially a cross-sectional design and included 2158 patients (1241 males and 917 females) undergoing HD in 25 hemodialysis units in six governorates in Egypt. The study started at June 2016 till May 2017. Data were extracted from the patients'

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records. One year mortality events in the included HD patients were prospectively observed and recorded.

Results: Males on HD had a significantly lower body mass index (BMI) values and were less efficiently dialyzed. Their blood pressure measurements were significantly higher. In addition, males had significantly higher serum albumin with a significantly lower serum potassium level. The overall mortality rate was 6.9% (149 deaths) during the one year follow up period with a significant male predominance (7.9% in males vs. 5.6% in females p=0.03). The mortality rate was highest within the first 14 months after starting hemodialysis therapy. Mortality was statistically significantly higher in patients with diabetes, ischemic heart disease (IHD), anemia with low hemoglobin, and low serum albumin. The mortality risk is nearly duplicated in HD patients with IHD, while low serum albumin was associated with about 3 times an increase in mortality risk in the studied HD patients.

Conclusion: Gender differences in clinical and laboratory characteristics and mortality do exist in Egyptian HD patients and should be considered when management guidelines are developed to suit the gender-related variations.

Keywords: Gender differences; morbidity; mortality; Egyptian hemodialysis.

1. INTRODUCTION

Chronic kidney disease (CKD) is an important cause of global morbidity and mortality affecting both sexes. There are tremendous human and economic implications with the progression of CKD to end-stage renal disease (ESRD). Mortality is as much as 17-fold higher in patients with ESRD compared to age- and gender-matched healthy individuals [1].

In Egypt, hemodialysis (HD) constitutes the most common modality of renal replacement therapy and the frequency of hemodialysis patients is increasing. Thus, between 2016 and 2017, the number of hemodialysis patients in Egyptian governmental health care service units is estimated to have increased from 23500 to 26000, respectively; with male to female ratio (1.6) [2].

Although dialysis therapy is hopefully meant to decrease the mortality and morbidity of patients with CKD stage 5, it seems that not all patients equally benefit from these merits of dialysis. Various factors, including increasing age, low body mass index (BMI), gender, diabetes mellitus as a cause of CKD, hemoglobin, ferritin, low serum albumin, low urea reduction ratio and coexisting illness like a left ventricular failure, ischemic heart disease, and hypertension are associated with changed risk of mortality in these patients [3-6].

Men and women with CKD may differ regarding the underlying pathophysiology of the disease and its complications. Both genders may present with different symptoms and signs, respond differently to therapy and may exhibit different degrees of tolerance towards their disease. However, there is a gender-based approach in the prevention and treatment of CKD, and implementation of clinical practice guidelines and research has largely been neglected [7].

The objectives of the present study were to investigate gender-related differences in clinical and biochemical characteristics in a representative sample of Egyptian HD patients and to explore the predictors of mortality in the total studied group.

2. PATIENTS AND METHODS

Many HD units, that we have experienced before their cooperation and accurate data provision, in different governorates in Egypt were approached and communicated to perform the study; however, only 25 HDUs in six governorates responded satisfactorily. This sample was utilized before in a previous research article about Ramadan fasting in Egyptian HD patients published in the Saudi Journal of Kidney Disease and Transplantation in 2019 [8]. This multicenter cross-sectional study included 2158 patients (1241 males and 917 females) undergoing HD in the 25 hemodialysis units; all patients in these HD units included without inclusion or exclusion criteria apart from being on HD for one month at least. The study started HD in June 2016 till May 2017. Demographic, clinical, and laboratory data were collected including; age, gender, duration of dialysis, associated comorbidities (diabetes mellitus, hypertension, ischemic heart disease, previous kidney transplantation, anemia, and CKD-MBD), and all routine investigations. Patients were prospectively observed for one year and mortality events were recorded.

Measurement of systolic and diastolic blood pressures was carried out before midweek dialysis sessions. Blood pressure was measured using an aneroid sphygmomanometer in the dialysis room. The mean of 3 consecutive readings was used in statistical analysis. The patient was assigned to have CKD-MBD when they had PTH values lower than 150 or higher than 700 pmol/L, had received cinacalcet (n=62), or had parathyroidectomy (n=32). Patients' dry body weights (the weight in which the patient has neither edema nor volume-dependent hypertension) and heights were obtained, and body mass index (BMI) for each patient was then calculated. Collected laboratory data included serum creatinine, serum urea, serum albumin, hemoglobin, serum ferritin, serum transferrin saturation (TSAT), serum calcium, serum phosphorus, and serum PTH. ELISA-based serological assessments for HCV, HBV, and HIV were also recorded. According to the current Egyptian Ministry of Health (MOH) recommendations, all patients were essentially dialyzed with a dialysate flow rate of ~500ml/min, blood flow rate ranging from 250-350 ml/min, and a total dialysis dose of 10-12 hours per week. All patients were dialyzed by a bicarbonate-based dialysis solution with a dialyzer surface area of 1.3-1.6 m2 made of Polysulfone or Helexone membrane material, sterilized with steam. In at least one-third of the treatment sessions, high flux membranes were utilized. Egyptian MOH guidelines were followed for water treatment in all the included HD units [9]. Urea reduction ratio (URR) was utilized to assess dialysis adequacy, being targeted to be above 60%.

2.1 Statistical Analysis

Data were collected, and statistical analysis was carried out by the "Statistical Package for Social Sciences" for Windows (SPSS), version "20". Test for normal distribution was performed using the "Kolmogorov-Smirnov test". Qualitative data were described as numbers and percentages. Chi-square ($\chi 2$) or Fisher Exact tests were used to compare qualitative variables, as appropriate. Quantitative data were described as means and standard deviations for normally distributed data or medians and ranges for non-normally distributed data. Independent "t"-test was used to compare two sets of normally distributed data, while the Mann-Whitney U test was used as a non-parametric equivalent. Logistic regression analysis was used to identify predictors of mortality with the calculation of odds ratio (OR; and 95% confidence interval, CI). The selected covariates for multivariate regression were the significant factors associated with mortality in bivariate analysis. The significant predictors only were highlighted in logistic regression.

3. RESULTS

The study population included 1241 males with a mean age of 52.2 years (±12.83) and 917 females with a mean age of 51.47 years (±13.49) with a male to female ratio of 1.35. Dialysis duration was 50.21 months (±40.02) in males and 52.05 (±48.76) in females There was no statistically significant difference in age at the start of HD and duration of dialysis between both genders. In all age groups, males slightly outnumbered females with no statistically significant difference. Systolic and diastolic blood pressure and dry body weight were statistically higher in males, while females showed statistically significantly higher BMI values. On the other hand, females had a lower frequency of HBsAg Table 1.

Table 2 shows a comparison of laboratory data between both genders. Serum albumin and urea were statistically significantly higher, while serum potassium and URR were lower in males**.** On the other hand, serum calcium, phosphorus, PTH and hemoglobin level, as well as serum ferritin and TSAT were not different in both genders. There was no statistically significant difference in all the studied comorbidities in both genders Table 3.

Mortality occurred in 6.9 % (149 deaths) of the observed HD patients during the one year follow up period. The mortality rate in males was 7.89 % (98 out of the 1241males) and 5.6% in females (51 out of the studied 917 females) with a statistically significant difference. Patients who were destined to mortality were older and had a lower duration of dialysis. On the other hand, patients aging above fifty-year were subjected to a higher mortality rate than those at or below this age. Diabetes and IHD were more commonly encountered in dead HD patients Table 4.

Mortality was statistically higher in the male gender, patients with diabetes, IHD, anemia with hemoglobin below 8.3 grams/dl, lower serum albumin (<3.0 gm/dl) and higher *serum calcium*. Although the mortality rate was highest in those patients with HD duration less than 14 weeks, the difference did not reach statistical significance Table 5.

In a trial to delineate predictors of mortality, a Logistic regression analysis was performed utilizing all studied variables that showed a statistically significant relation with mortality and the only significant predictors were represented in Table 6. It is notable that both serum albumin and IHD, as a co-morbidity, as well as corrected serum calcium were significant predictors for mortality, with the odds ratios as shown in the table. On the other hand, logistic regression analysis that was performed on females' and males' groups separately showed that IHD is the only significant predictor of mortality among females' group, however this analysis could not explore the predictor of mortality among males' group Tables 7a and 7b respectively.

4. DISCUSSION

The prevalence of CKD was observed to be greater in women than in men regardless of age distribution [10-16] However, in hemodialysis units, males outnumber females [17] In harmony with that, there is a higher number of Egyptian male gender undergoing hemodialysis. [Unpublished data]. Nevertheless, studies addressing female to male-specific differences in pathophysiology, progression, management, and

Table 1. Demographic, clinical and serological characteristics of both genders

Demographic data				
Age groups in years		**Females (n=917) N (%)**	**Males (n=1241) N (%)**	**P value**
15-34		119(13)	136(11)	0.5
35-54		380(41.4)	521(42)	
55-74		394(43)	553(44.6)	
75-90		24(2.6)	31(2.5)	
Age (Mean ±SD) in years		51.473±13.5	52.2±12.83	0.1
Duration of dialysis (months)	**Mean**	52.05	50.2	0.4
	Median	38	36	
	Min. – Max.	1-258	1-307	
Age at start of dialysis in years (Mean ±SD)		47.12±14.2	47.9±13.8	0.1
Clinical variables:				
		Females Mean ±SD	**Males Mean ±SD**	**P value**
Pre dialysis session SBP (mmHg) *Female/*Male (809/1093)		131.267 ±25.21	133.58 ±20.565	0.02
Pre dialysis session DBP (mmHg) *Female/*Male (809/1095)		80.9 ±10.1	82.25 ±10.775	0.006
Dry body weight *Female/*Male (876/1212)		70.6 ± 17.5	73.5 ± 16.1	<0.001*
Body mass index (BMI) *Female/*Male (287/445)		26.7 ±6.3	25.4± 5.4	0.004
Serological data				
Serology		**Female No (%)**	**Male No (%)**	**P value OR (95%CI)**
Normal (r)		576 (62.8)	722 (58.2)	
Anti-HCVAb		324 (35.3)	458 (36.9)	0.1 0.89(0.74-1.07)
HbsAg		9 (1.0)	41 (3.3)	<0.001 0.28 0.12-0.59)
Combined anti-HCV Ab &HBsAg		6 (0.7)	20 (1.6)	0.03 0.38(0.13-1.0)
Anti-HIV Ab		2 (0.2)	0 (0)	0.19 OR Undefined
Total		917 (100%)	1241 (100%)	

SBP= systolic blood pressure, DBP= diastolic blood pressure, BMI= body mass index, HCV= hepatitis C virus, HBV= hepatitis B virus, Ab= antibody, Ag= antigen

** Represents the number of the available data*

(r): reference group, OR (95%CI): Odds ratio (95% confidence interval)

Table 2. Comparison of laboratory data in both genders

		Female		Male		
		N	Mean ±SD or Median (Min-Max)	N	Mean ±SD	P value
Hemoglobin gm/dL		856	9.5±1.8	1157	9.7± 1.8	0.06
Serum Creatinine mg/dL	**Median**	476	7.5	199	7.8(686)	0.10
	Min – Max		2.8-17		2.2-17	
Urea, mg/dL		789	123.7± 34.5	1017	129.9±36.6	<0.001
URR		741	0.61	963	0.59	0.01
Serum Calcium, mg/dL		512	8.7±1.5	674	8.8±1.5	0.10
Corrected Serum Calcium, mg/dL		374	8.9±1.5	490	9.06 ±1.5	0.40
Serum Phosphorus, mg/dL		494	5.16±1.376	651	5.26±1.46	0.20
Serum potassium mEq/L		156	5.2±1.3	230	4.9±1.04	0.03
Serum Albumin, gm/dL		535	3.7±0.7	743	3.8± 0.6	0.04
Serum PTH, pg/mL	**Median**	312	321.5	408	306.9	0.40
	Min – Max		4.7-2265.9		8-2503	
Serum Ferritin, ng/mL	**Median**	273	590.0	358	469.5	0.10
	Min – Max		17.7-1997		19.8-2237	
Transferrin saturation %	**Median**	129	32.0	139	30.0	0.40
	Min -Max		6.64.1		8-64.0	
PTH categories, pg/mL		N	%	N	%	
<150		82	26.3%	107	26.2%	0.50
150-700		155	49.7%	216	52.9%	
>700		75	24%	85	20.8%	
Total		312	100%	408	100%	

URR= urea reduction ratio PTH; parathyroid hormone

Table 3. Comparison of associated comorbidities in both genders

	Female (n=917)	Male (n=1241)	p value, OR (95%CI)
DM, n(%)	190 (20.7%)	222 (17.9%)	p=0.09, OR=0.8(0.6-1.03)
Hypertension, n(%)	409 (44.6%)	594 (47.9%)	p=0.10, OR=1.14(0.9- 1.35)
IHD, n (%)	198 (21.6%)	302 (24.3%)	p=0.10. OR=1.16(0.95-1.4)
Previous kidney transplant, n(%)	7 (0.8%)	19 (1.5%)	p=0.10, OR=2.02(0.8-4.8)
Hemoglobin, ≤9gm/dL(≤90gm/L), n (%)	350 (40.9%)	430 (37.2%)	p=0.09, OR=0.8(0.7-1.02)
CKD-MBD, n (%)	190 (56.2%)	218 (51.2%)	p=0.10, OR=0.8(0.6-1.08)

DM= diabetes mellitus IHD= ischemic heart diseases CKD-MBD= chronic kidney disease-mineral bone disorder

outcomes in patients with different stages of CKD are still lacking in randomized clinical trials [7]. Since the insights toward personalized treatment strategies are encouraged by many of the available guidelines in medical practice, while this may have been largely overlooked by the main body of hemodialysis guidelines (KDOQI), we thought that gender difference should not be ignored or neglected while providing hemodialysis healthcare service.

In the current study, males constitute 57.5 % of the studied population. Our results showed nearly similar mean age, similar age at the start of HD, and similar mean dialysis duration in both genders. A higher number of males on hemodialysis was previously reported by many national and international reports [17-21]. This could be attributed to the faster CKD progression among males [22,23].

Gender-related differences in blood pressure measurements in patients on hemodialysis need to be clarified. Few studies have addressed this issue in hemodialysis patients; in a Nigerian study, Okaka et al, found that females had higher DBP values [24]. Data from the current study indicate that blood pressure measurements (systolic and diastolic) were significantly lower in females. However, the difference is of limited clinical importance.

The association of a higher body mass index (BMI) with better survival is a well-known "obesity paradox" in patients on HD. Many reports addressed BMI gender differences with contradictory results. Jeung and his colleagues found no significant difference in BMI values among different genders. However, men and women have different body compositions, which could impact the effect of BMI on mortality. They found that BMI could be used as a risk factor for mortality in male patients, not in female patients, on HD [20]. Results from the current study matched those reported by previous publications who found lower BMI values among males [16, 17] It is well-known that men and women have different proportions of skeletal muscle and fat mass that could affect BMI and serum creatinine level in HD patients [25]. Higher BMI values that were found in females are mostly related to higher fat mass which could denote poor rather than a good state of nutrition. This should be further documented by analyzing body composition and fat distribution in males and females on hemodialysis. Besides, URR values were found to be higher in females in the current work which may be explained by their exposure to the same dialysis dose with body weights and surface areas much lower than males. Depner and his colleagues have theorized that men are well-known to be larger than women and thus may require a higher dialysis dose to achieve the same dialysis adequacy [26]. Weigert and his associates found that body weight and the prescribed dialysis blood flow rate were lower in women (< 0.001), whereas treated blood volume per kilogram per session was higher (< 0.01), resulting in higher single-pool Kt/V in women than in men (< 0.001) [27].

Female patients in the current study have significantly higher serum potassium levels, the reason for this is unclear, however, it might be possible that lack of compliance toward eating potassium-containing foods could be higher among females. In harmony with that, Takaki and Yano previously reported poorer compliance and adherence to food restrictions and hence higher potassium levels among the female group [28].

Although the prevalence of Hepatitis B virus (HBV) in patients with end-stage renal failure (ESRF) who are undergoing dialysis has decreased significantly over the past few decades, it remains a distinct clinical problem. It was reported that the prevalence of positive HBsAg among Egyptian hemodialysis patients ranges from 2%–7%. [29] This is consistent with our results that showed that 3.5% of our population had positive HBsAg. The prevalence of HBsAg is lower in the female group in our

Table 4. Comparison between alive and dead groups according to demographic and clinical data

	Mortality				P value
	No, n=2009		Yes, n=149		
	N	Mean±SD or Median (Min–Max)	N	Mean±SD or Median (Min–Max)	
Age/years (mean±SD)	2008	51.58 ±13.14	149	56.2 ±12.08)	<0.001
BMI kg/m^2 (mean±SD)	674	25.9253 ± 5.84	58	26.132 ±5.63	0.7
Duration of dialysis, months [Median (Min–Max)]	1983	29.5 (1-307)	141	37(1-258)	0.06
Pre dialysis SBP, mmHg, (mean±SD)	1777	81.7 (10.4)	127	81.378 (11.7)	0.7
Pre dialysis DBP, mmHg, (mean±SD)	1775	132.595 (22.77)	127	132.675 (21.5)	0.9
Associated comorbidities					
N* Number of alive patients/ Number of dead patients	**N(%)**	**N(%)**	**P value, OR (95%CI)**		
DM N* 209/149	368 (18.31%)	44 (29.5%)	P=0.001, OR=1.86 (1.3-2.7)		
Hypertension N* 209/149	933 (46.4%)	70 (46.9%)	P=0.8, OR=1.02 (0.7-1.4)		
IHD N* 209/149	442 (22%)	58 (38.9%)	P<0.001, OR=2.3 (1.6-3.2)		
Previous kidney transplant N* 209/149	26 (1.2%)	0 (0%)	P=0.16, OR=0.9 (0.9-0.9)		
CKD-MBD N* 680/40	418 (61%)	24 (60%)	P=0.9, OR=0.9 (0.5-1.8)		

BMI= body mass index, SBP= systolic blood pressure, DBP= diastolic blood pressure, DM= diabetes mellitus, IHD= ischemic heart diseases, CKD-MBD= chronic kidney disease-mineral bone disorder, N= represents the number of the available data*

Table 5. Associated factors with mortality (Bivariate analysis)

		Mortality		P value OR(95%CI)
		No Mean (SD) or N(%)	Yes Mean (SD) or N(%)	
Age/years	N	2009	149	0.001 [1.8(1.2-2.5)]
	≤50 (r)	866(95.2%)	44(4.8%)	
	>50	1143(91.5%)	105(8.5%)	
Gender	N	2009	149	0.03 [1.46(1.01-2.1)]
	Female	866(94.4%)	51(5.6%)	
	Male	1143(92.1%)	98(7.9%)	
Duration of Dialysis/months	N	1983	140	
	< 14	500(91%)	48(9%)	0.09 [1.5(0.9 -2.4)]
	14-36	470(93%)	35(7%)	0.5[1.15(0.68-1.95)]
	37-72	517(95%)	25(5%)	0.29[0.75(0.42-1.32)]
	≥72 (r)	496(94%)	32(6%)	1
Hemoglobin gm/dL	N	1880	133	
	<8.3	456(88.8%)	57(11.1%)	0.0006[2.2(1.36-3.6)]
	8.4-9.5	431(95.1%)	22(4.9%)	0.7[0.9(0.49-1.6)]
	9.6-10.7	481 (95.1%)	25(4.9%)	0.7[0.9(0.51-1.64)]
	≥10.8 (r)	512(94.6%)	29(5.4%)	1
Corrected Serum Calcium mg/dL		N=808	N=56	0.002
		8.9±1.5	9.6±1.4	
Serum Phosphorus mg/dL		N=1075	N=70	0.9
		5.2±1.4	5.2±1.5	
Serum Phosphorus categories mg/dL	<2.5	14 (100%)	0% (0 %)	0.6
	2.5-4.5	348 (93.8%)	23 (6.2%)	
	>4.6	713 (93.8%)	47 (6.2%)	
	Total	1075 (93.88%)	70 (6.12%)	
Serum Albumin categories gm/dL	N	1202	76	
	<3	142(87.6%)	20(12.4%)	0.0005[3.13(1.7-5.7)]
	3-3.5	281(93%)	21(7%)	0.07[1.6(0.9-3.0]
	>3.5 (r)	779(95.7%)	35(4.3%)	1
PTH categories pg/mL	N	680	40	
	<150	176(93.2%)	13(6.9%)	0.5[1.23(0.57-2.6)]
	150-700 (r)	350(94.3%)	21(5.7%)	1
	>700(225.8)	154(96.3%)	6(3.7%)	0.3[0.6(0.23-1.74)
Ferritin categories ng/mL	N	593	38	
	<513	300(94.6%)	17(5.4%)	0.4[0.8(0.4-1.6)]
	≥513 (r)	293(93.3%)	21(6.7%)	1
URR categories	≤0.6	819(93.6%)	56(6.4%)	0.1
	>0.6	355(95.9%)	15(4.1%)	
	Total	1174	71	

URR= urea reduction ratio ; PTH= parathyroid hormone

studied hemodialysis population. A previous Australian report has found that males have a higher prevalence of positive HBsAg than females [30] which could be explained by more exposure of males to risk factors of HBV transmission, shaving at Barber's, more exposure to accidents, drug abuse, etc. It also was reported that females are more likely than males to produce anti-HBs antibodies in response to infection [31].

In the general population, females are known to have lower hemoglobin than males which is attributable to different factors e.g.: lack of androgens and iron deficiency related to menstrual losses [32] In the current work, hemoglobin level, serum ferritin, and TSAT were comparable in both genders. Lower hemoglobin levels among females on HD were reported by many authors [16,33,34]. Hecking and his colleagues reported lower hemoglobin levels

despite higher EPO doses given to females [16]. Although the normal range of hemoglobin and diagnosis of anemia is known to be different between men and women [32], most of the international organizations and guidelines do not differentiate between the target level of hemoglobin in hemodialysis patients in both genders [35]. It might be speculated that hemodialysis females would not need a target hemoglobin level as high as that of their corresponding males to function similarly. Therefore, extensive studies are needed to explore which value of target hemoglobin should be in both genders.

It would be of interest to see whether comorbidities associated with CKD have gender differences. In the current work, DM was more frequent in females although not reaching the level of statistical significance; a finding which is consistent with previous publications [16,17]. Some authors demonstrated a high prevalence of DM among female patients [36]; a situation that appears to be parallel to that present in the studied HD population in the current study. Of note, the frequency of other CKD associated comorbidities named hypertension, IHD and CKD-MBD were not different between both genders.

In the last few decades, hemodialysis modalities and health care service had improved dramatically. Despite this evolution in hemodialysis service, mortality rates are still considerably high. Few studies have addressed factors predicting mortality in the hemodialysis population in different localities including Egypt.

Table 6. Predictors of Mortality among studied patients (Logistic regression analysis)

Predictors		β	P	OR(95%CI)
Albumin gm/dL	<3	1.35	0.001	3.8 (1.8-8.1)
	3-3.5	0.65	0.04	1.9 (1 -3.6)
	>3.5 (r)			1
IHD	No			1
	Yes	0.73	0.01	2.08 (1.2-3.6)
Corrected serum Calcium		0.25	0.009	1.3 (1.06-1.5)
Constant		-5.6		
Percent correctly predicted		93.5		
Model χ^2		28.2; P≤0.001		

IHD; ischemic heart disease

Table 7a. Predictors of Mortality among Females' group (Logistic regression analysis)

Predictors	B	Sig.	Exp(B)	95% C.I. for EXP(B)	
				Lower	Upper
Age	.035	.135	1.035	.989	1.083
DM	-.119-	.849	.888	.261	3.023
IHD	1.108	.046	3.029	1.019	9.010
CKD-MBD	.212	.359	1.236	.786	1.945
Constant	-5.622-	.000	.004		

DM= diabetes mellitus, IHD= ischemic heart disease, CKDMBD= chronic kidney disease mineral bone disorder

Table 7b. Predictors of Mortality among Males' group (Logistic regression analysis)

Predictors	B	Sig.	Exp(B)	95% C.I. for EXP(B)	
				Lower	Upper
Age	.006	.733	1.006	.973	1.039
Hemoglobin	.006	.956	1.006	.817	1.238
Serum phosphorus	-.086-	.585	.918	.675	1.248
IHD	.609	.176	1.838	.762	4.434
BMI	.024	.534	1.025	.949	1.106
Constant	-3.106-	.071	.045		

IHD= ischemic heart disease, BMI= body mass index

During the one year follow up study period, we recorded 149 deaths out of 2158 HD patients in which males constitute the majority. In the general population, the male-to-female mortality ratio varies from 1.5 to 2.6 for age groups <75 years [37]; this female advantage markedly diminished in the setting of hemodialysis and the ratio becomes close to one [16]. Males in our study appeared to have higher mortality than females; a finding that is consistent with previous reports that found a significantly poorer survival rate in males [18,38]. On the contrary, some authors reported almost equal mortality ratios among both genders [16,39], while others reported an even poorer mortality rate among females [40]. These heterogeneous results may be due to different population, and different clinical criteria of included samples.

In the current research, Mortality was observed in patients with older age especially those with the age of more than 50 years, patients with diabetes or IHD and those with lower serum albumin or lower hemoglobin levels. The association of higher risk of mortality and later risk factors was reported by many authors [7, 18,38,41]. Cardiovascular disease was previously found to be the most leading cause of mortality among the hemodialysis population [42-44]. Hypoalbuminemia is highly prevalent in kidney failure and is associated with an increased risk of mortality among this population. Hypoalbuminemia may reflect either poor nutritional status or degree of inflammation in patients with ESRD on hemodialysis [44,45].

The highest mortality rate in this study was reported within the first 14 months after starting hemodialysis therapy; a nearly similar result was reported by Robinson and his colleagues, who found that the early hemodialysis period is a high-risk for death in hemodialysis patients [46]. It was reported that early period of dialysis may be associated with a higher incidence of catheter-related complications [47], poor general condition (e.g.: volume overload, and hypoalbuminemia related to poor nutritional state), especially for whom with late dialysis referral [48].

Interestingly, we found higher corrected serum calcium values among the dead group, a finding which is in concordance with previous reports [38,41,48-52]. The decreased excretion rate of calcium, the abuse of vitamin D and calcium-based phosphate binders, and hyperparathyroidism that occur in ESRD contribute largely to the occurrence of hypercalcemia and consequently the development of CV calcification. Even the subclinical hypercalcemia (ie; normal corrected serum calcium with high ionized calcium) was found to be associated with greater risk of mortality as reported by Obi and his coworker [53]. High serum calcium, low serum albumin, and the presence of IHD were the most significant predictors of mortality in the whole sample. The presence of IHD as the only predictor of mortality among the females' rather in the males' group, raises the thinking that this co-morbidity could behave differently among both genders. Tomaszewski and his colleagues have reported that IHD carries a poorer quality of life and adverse outcomes in females than males owing to different biological and pathological factors [54]. However, this observation is not settled yet in the hemodialysis population. Eun Ko and his colleagues concluded that ‘mild to severe malnutrition’ was significantly correlated with increased mortality. ‘Mild to severe malnutrition’ was significantly associated with increased mortality in male patients. However, there were no significant associations between the state of nutrition and mortality for female patients [55]. Generally, gender differences as regards the treatment of patients with hemodialysis and morbidity and mortality risk during HD have been taken in the nephrologists’ society consideration. These differences could be attributed to biological factors (hormonal and genetic factors), work hazard exposures, national and social policies about patient care, etc. This speculation needs comprehensive studies on large scales.

4.1 Strength and Limitations of the Study

The current study is one of the largest prospective studies conducted on hemodialysis patients in Egypt, and none of the available national reports provides a comprehensive analysis of gender-related differences or mortality predictors among those patients.

One important limitation in the present study is the failure to define specific etiology of CKD and direct causes of death and their effect on mortality. Another weak point resides in the lack of determination of differences in body composition and their relation to the dose of dialysis in both genders. Another adding weak point is that clinical and laboratory parameters measured only at the onset of the study, although multiple measurements of these parameters would be more conclusive.

5. CONCLUSION

Gender-related differences in HD patients have been appreciated in the present study; males had lower BMI values, higher blood pressure measurements, lower dialysis dose, and more HBV infection, while females had lower serum albumin, lower hemoglobin, and higher serum potassium levels. Mortality afflicted 6.9% in the studied population with significant male predominance. Mortality was more frequently observed in older age>50 years, presence of IHD and DM, higher serum calcium, and lower serum albumin. The effect of gender on mortality in hemodialysis patients' needs to be further investigated concerning specific causes of death and the etiology of CKD.

6. RECOMMENDATIONS

The gender-related difference should be considered in future management guidelines of hemodialysis patients. Both genders may present with different symptoms and signs, respond differently to therapy with different degrees of tolerance towards the disease. The gender-based approach in the prevention and treatment of CKD, and also the implementation of clinical practice guidelines and research related to gender need more consideration. Treatment guidelines could be tailored for each gender.

CONSENT

Consent was obtained from each study participant.

ETHICAL APPROVAL

All procedures were approved by the research ethics committee at the ministry of health, Egypt and carried out under Mansoura University Hospital guidelines.

DATA AVAILABILITY

All data generated or analyzed during this study are included in this published article.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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