

Published by Al-Nahrain College of Medicine ISSN 1681-6579 Email: iraqijms@colmed-alnahrain.edu.iq http://www.colmed-alnahrain.edu.iq

Erectile Dysfunction in Haemodialysis Patients in Al-Imamain Al-Kadhemain Medical City and Al-Kindy Teaching Hospitals

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Abstract

Background Erectile dysfunction is the inability to attain or maintain an erection sufficient for satisfactory sexual

performance. There is a very high prevalence among dialysis patients. Many factors play a role including

the disease itself and dialysis.

Objective To identify the rate of erectile dysfunction in uremic patient undergoing haemodialysis and to find the

association between the erectile dysfunction and many confounding factors.

Methods All male patients of end stage renal disease were kept on maintenance haemodialysis therapy. Patients

were divided into two groups according to the International index of erectile function-5, first group with erectile dysfunction with score of 21 and less, the second group without erectile dysfunction with score

of 22 and more.

Results The percentage of erectile dysfunction in the study sample was (84.9%). Factors responsible for erectile

dysfunction are diabetes mellitus (73.3%), increasing age (75.5%) of patients, high predialysis urea level (82.2%), smoking, hepatitis B and C virus infection, systolic blood pressure, albumin, creatinine,

haemoglobin and the duration of dialysis are not related.

Conclusion Majority of the patients with end stage renal disease on maintenance haemodialysis have higher rate of

erectile dysfunction. Major factors responsible for erectile dysfunction are diabetes mellitus, increasing

age and high predialysis urea.

Keywords Haemodialysis, erectile dysfunction, International index of erectile function-5.

List of abbreviations: CKD = Chronic kidney disease, ED = Erectile dysfunction, DM = diabetes mellitus, Hbsag = Hepatits b surface antigen, HCV ab = Hepatitis C virus antibody, HD = Hemodialysis, IIED-5 = International index of erectile function.

Introduction

hronic kidney disease (CKD) in adults is defined by The Kidney Disease Outcomes Quality Initiative (K/DOQI) as structural and/or functional kidney abnormalities (abnormal urinalysis, imaging studies, or histology) that persist for at least three months (1-2). CKD has been classified into five stages according to the degree of the glomerular filtration rate (3-4). Sexual dysfunction in CKD

includes erectile dysfunction (ED), decreased libido and marked decrease in the frequency of intercourse ⁽⁵⁾.

ED is defined as the consistent or recurrent inability to acquire or sustain an erection of sufficient rigidity and duration for sexual intercourse ⁽⁶⁾. In general, ED is present in up to 30 million men in the United States and approximately 100 million men worldwide ⁽⁷⁰⁾. Patients of CKD have prevalence of ED ranging from approximately 50 to over 90% ^(8,9). ED may result from three basic mechanisms failure to initiate, to fill and to restore the function of cavernous muscle ⁽¹⁰⁾.

In addition to age, the best predictors of ED are diabetes mellitus (DM), hypertension, obesity, dyslipidemia, cardiovascular disease, smoking, and use of medication, psychosocial disease, neurological and endocrine disorder (11-13). The association of cardiovascular disease and ED is due to sharing many risk factors and both mediated pathophysiology is through endothelial dysfunction (14-16). The management of uremic men with sexual dysfunction begins by maximizing the delivered dose of dialysis, discontinuing medications (if possible), correcting the anaemia of chronic renal disease, example, the administration as an recombinant human erythropoietin to raise the hematocrit to 33 to 36 percent may enhance sexual function (17).

Different treatment strategies known at the time being for treatment of ED; phosphodiesterase inhibitors I, Psychotherapy and/or psychoactive medications ⁽¹⁸⁻²⁰⁾.

The aim of the study to identify the prevalence of ED in uremic patients undergoing haemodialysis and to find the relationship between the ED and certain confounding factors.

Methods

A descriptive case – series study conducted from the 1st of November 2011 to the 31st of January 2012 in the Haemodialysis unit of Al-Imamain Al-Kadhemain Medical City and Al-Kindy Teaching Hospital in Baghdad city.

Fifty-three male patients who were on regular maintenance haemodialysis were included in the study. Only those patients who had live spouses were included. Their age range was 18 to 75 year. The marital sex is considered as an appropriate expression of sexuality.

Exclusion criteria: Patients of acute renal failure and those with cognitive/communication deficit. All patients were informed and consent about the study was taken. Each subject completed a self-administered 5-item validated questionnaire

(21), the International Index of Erectile Function (IIEF-5), adapted in Urdu (22) which is a bridged version of the 15-item International Index of Erectile Function (23). On the basis of IIEF-5, categorisation of ED was done into those with the ED (with score of 21 and less) and without ED for those with score 22 and more (total score =25).

Data was analysed dividing the patients into ED and None ED groups. Demographic data was collected on a forma containing age, duration of dialysis, history of smoking and of DM. At the same time blood pressure was checked and blood sample of these patients was drawn to measure blood (urea, creatinine, blood sugar, albumin, HBs Ag, Anti HCV).

Data was entered and analysed using SPSS 16.0. Mean \pm SD is given for normally distributed quantitative variables. Frequencies and percentages are given for qualitative variables. Pearson Chi square test was applied to observe correlations in qualitative variables. A P < 0.05 was considered statistically significant.

Results

Table 1 show the demographic data of the 53 patients studied that includes the mean of the age of patients was 38.79 ± 9.03 years. IIEF-5 score: 45 patients (84.9%) have IIEF-5score less than 22 (they have ED), 8 patients (15.1%) have IIEF-5 score equal to or more than 22 (they did not have ED).

The mean age of those patients with ED was 38.93 ± 8.84 years, which is significantly higher (P < 0.05) than 30.63 ± 4.17 years of patients without ED. The mean urea level for patients with ED was 179.09 ± 32.03 mg/dl, which is significantly higher (P < 0.05) as compared 138.9 ± 38 mg/dl for patients without ED.

Concerning albumin, systolic blood pressure, creatine level, Hb level and mean duration of dialysis, they were not different between the two groups (Table 2).

Table 1. Demographic data of the patients included in the study

Feature	Category	No.	%	Mean
Age (years)	< 35	17	32.1%	
	35-44	24	45.3%	38.79 ± 9.03
	≥ 45	12	22.6%	
	< 150	14	26.4%	
Urea level (mg/dl)	150-189	21	39.6%	173.0 ± 35.69
	≥ 190	18	34.0%	
	< 2.5	14	26.4%	
Albumin level (g/dl)	2.5-3.4	26	49.1%	2.95 ± 0.64
	≥ 3.5	13	24.5%	
	< 140	4	7.5%	
Systolic BP (mmHg)	140-179	23	43.4%	168.8 ± 25.1
	≥ 180	26	49.1%	
	< 4	2	3.8%	
Creatinine (mg/dl)	4-7.9	38	71.7%	6.65 ± 1.53
	≥8	13	24.5%	
Direction of dishusis	< 17	24	45.3%	
Duration of dialysis	17-22	17	32.1%	19.91 ± 7.32
(months)	≥ 23	12	22.6%	
	< 7	4	7.5%	
Hb (g/dl)	7-10	39	73.6%	9.28 ± 1.77
	≥ 10	10	18.9%	
Diahataa mallitus	Yes	34	64.2%	
Diabetes mellitus	No	19	35.8%	
LID-AI-I-	Negative	47	88.7%	
HBsAg state	Positive	6	11.3%	
11C\/ab -+-+-	Negative	38	71.7%	
HCVab state	Positive	15	28.3%	
	Non smoker	23	43.4%	
Smoking	ex-smoker	22	41.5%	
	smoker	8	15.1%	
UEE E coore	< 22	45	84.9%	
IIEF-5 score	≥ 22	8	15.1%	

BP = Blood pressure, IIEF-5 = International Index of Erectile Function

Table 2 showed quantitative variables of patients found with and without ED. Thirty three patients who were diabetics at the same time presented with ED. A value that significantly higher (P < 0.05) than only uremic patients who had no ED. Concerning smoking habit, HBsAg positive and anti HCV positive, no significant

difference was noted between those with and without ED (Table 3).

Table 4 show relationship between ED and certain confounding factors It was evident that blood urea, Diabetes mellitus and the age of patients were significantly associated with ED (*P* < 0.05), on the contrary albumin level, creatinin level, systolic blood pressure, Hb level, smoking

habit, HBsag state and HCVab state showed no significant association with ED.

Table 2. Quantitative variables of patients with and without erectile dysfunction

	Erectile d			
Feature	Yes (Mean ± SD)	No (Mean ± SD)	P value	
	N = 45	N = 8		
Age (years)	38.93 ± 8.48	30.63 ± 4.17	< 0.05	
Urea level (mg/dl)	179.09 ± 32.03	138.9 ± 38	< 0.05	
Albumin level (g/dl)	2.91 ± 0.62	3.61 ± 0.51	> 0.05	
Systolic BP (mmHg)	170.2 ± 25.5	161.2 ± 22.9	> 0.05	
Creatinine (mg/dl)	6.47 ± 1.47	7.71 ± 1.53	> 0.05	
Duration of dialysis (months)	19.73 ± 7.55	20.88 ± 6.20	> 0.05	
Hb (g/dl)	9.16 ± 1.79	9.92 ± 1.65	> 0.05	

BP = Blood Pressure, Hb = Hemoglobin

Table 3. Qualitative variables of patients with and without erectile dysfunction

		Erectile o			
Variable		Yes (Mean ± SD) No (Mean ± SD) N = 45 N = 8		P value	
Current smokers		7	1	< 0.05	
HBsag positive		5	5 1		
Anti HCV positive		13	2	> 0.05	
Diabetes mellitus	Yes	33	1	40.05	
	No	12	7	< 0.05	

DM = diabetes mellitus, ED = erectile dysfunction

Discussion

ED is a major health issue in modern life, impact on quality of life (24). In this study, there is very high prevalence (84.9%) of ED in haemodialysis patients, which is similar to that observed in Iran (87.5%) (25), Turkey (82.9%) (26), Egypt (82.5%) (27) and Brazil (86.4 %) (28). Factors responsible for such a high rate of ED in dialysis patients in current study is related with multiple factor including DM, increasing age (more than thirty five years) and very high pre dialysis urea level. The current study showed that the ED was more prevalent in diabetic than non diabetic patients and it reveals significant association. Similar result is observed by Miyata et al (29). DM affects ED in many ways. Large vessel atheromatous disease is 40 times more prevalent amongst men with diabetes compared to non-diabetics ⁽³⁰⁾. DM causes ultra structural changes in cavernosal tissues, these changes including reduction in smooth muscle content, increased collagen deposition, thickening of basal lamina and loss of endothelial cells ⁽³¹⁾, and finally endothelial and neurogenic relaxant responses mediated by nitric oxide are impaired in diabetes mellitus ^(31,32)

In the current study, increasing age significantly correlated with the prevalence of ED, which is in agreement with other studies like the Massachusetts Male Aging (MMA) study ⁽³³⁾, Rodger et al ⁽³⁴⁾, Chun–Fu Lia et al ⁽³⁵⁾ and Rosas et al ⁽³⁶⁾ found a strong association between age and prevalence of ED.

Table 4. The relationship between the urea, albumin, SBP, creatinine, duration of the dialysis, age,
Hb and erectile dysfunction

Parameters		With ED		Without ED		Total		
		No.	%	No.	%	No.	%	P value
A == (va = va)	< 35	11	24.4	6	75	17	32.1	
	35-44	23	51.1	1	12.5	24	45.3	< 0.05
Age (years)	≥ 45	11	24.4	1	12.5	12	22.6	< 0.03
	total	45	100	8	100	53	100	
	< 17	21	46.7	3	37.5	24	45.3	. 0.05
Duration of haemodialysis	17-22	14	31.3	3	37.5	17	32.1	
(months)	≥ 23	10	22.2	2	25	12	22.6	> 0.05
	total	45	100	8	100	53	100	
	> 150	8	17.8	6	75	14	26.4	
	150-189	20	44.4	1	12.5	21	39.6	40.0F
Urea level (mg/dl)	≥ 190	17	37.8	1	12.5	18	34.0	<0.05
	total	45	100	8	100	53	100	
	<2.5	12	26.7	2	25	14	26.4	<0.05
Albumin level (g/dl)	2.5-3.4	23	51.1	3	37.5	26	49.1	
Albumin level (g/di)	>=3.5	10	22.2	3	37.5	13	24.5	
	total	45	100	8	100	53	100	
	< 140	3	6.7	1	12.5	4	7.5	<0.05
Systolic BP (mmHg)	140-179	19	42.2	4	50	23	43.4	
Systolic Br (Illiling)	≥ 180	23	51.1	3	37.5	26	49.1	
	total	45	100	8	100	53	100	
	< 4	2	4.4	0	0	2	3.8	<0.05
Creatining level (mg/dl)	4-7.9	34	75.6	4	50	38	71.7	
Creatinine level (mg/dl)	≥ 8	9	20	4	50	13	24.5	
	total	45	100	8	100	53	100	
	< 7	4	8.9	0	0	4	7.5	>0.05
Hb level (g/dl)	7-10	33	73.3	6	75	39	73.6	
Hb level (g/ai)	≥ 10	8	17.8	2	25	10	18.9	
	total	45	100	8	100	53	100	

The average age of this patient with ED was 50 years and 38 years for those without ED (P < 0.001). While in the present study, the mean of the age of patients with ED was 38.9 years and 30.6 years for patients without ED. This difference may be related to other factors like dialysis techniques, medications (like antihypertensive medications) and psychological state.

Age causes gradual changes in sexual organs; these changes do not occur suddenly like women but occurs gradually during a process called andropause or late onset hypogonadism (37). An abrupt increase in hypogonadism prevalence occurred in men aged 45 to 50 years beyond which a plateau of prevalence was maintained until older than 80 year of age (38). In present study, the blood urea level in patient with ED was higher in those with ED; similar result was observed by Mumtaz et al (39). Increased urea level leads to decreased synthesis of nitric oxide and super saturation of the oxygen free radicals, these oxygen free radicals lead to increased consumption of nitric

oxide, which is a relaxing factor for penile smooth muscles (40).

Table 5. The relationship between the HBs Ag, HCVAb, diabetes mellitus, smoking and erectile dysfunction

Parameters		With ED		Without ED		Total		P value
		No.	%	No.	%	No.	%	P value
	Negative	40	88.9	7	87.5	47	88.7	
HBsag state	Positive	5	11.1	1	12.5	6	11.3	> 0.05
	Total	45	100	8	100	53	100	
	Negative	32	71.1	6	75	38	71.7	
HCVab state	Positive	13	28.9	2	25	15	28.3	> 0.05
	Total	45	100	8	100	53	100	
Diabetes mellitus	No	12	26.7	7	87.5	19	35.8	
	Yes	33	73.3	1	12.5	34	64.2	< 0.05
	Total	45	100	8	100	53	100	
Smoking	Non smoker	19	42.2	4	50	23	43.4	> 0.0F
	Ex-smoker	19	42.2	3	37.5	22	41.5	
	Smoker	7	15.6	1	12.5	8	15.1	> 0.05
	Total	45	100	8	100	53	100	

In the present study, the systolic blood pressure and serum albumin level show no significant association with ED (P > 0.05), this result is comparable to Mumtaz et al study ⁽³⁹⁾.

The mean duration of dialysis, s. creatinin level and Hb level, smoking habit and HBsag have nothing to do with ED, findings in accordance with Steel et al ⁽⁴⁰⁻⁴¹⁾, Messina et al ⁽⁴²⁾, Leila et al ⁽⁴³⁾, and Mumtaz et al ⁽³⁹⁾ current study the HBsag state has non significant association with FD.

In conclusion, majority of the patients suffering from ED, on maintenance haemodialysis are having ED, haemodialysis does not improve sexual dysfunction, and major factors responsible for ED are diabetes mellitus, age more than 35 years and high pre dialysis urea.

The limitation of the study was lack of control group; follow up was not done which would have been useful to determine small size, and assessment of sex hormones

Acknowledgments

We would like to express our thanks and gratitude to the medical staff of the dialysis unit

in the Al-Imamain Al-Kadhimain Medical City and to the patients who accept to be involved in the study.

Author contribution

The first author involved in the collection of samples, arrangement and writing of the study under the supervision of the second author.

Conflict of interest

The authors declare no conflict of interest.

Funding

Personal

References

- National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002; 2002; 34 39-51.
- 2. Levey AS, Eckardt KU, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: a position statement from[9a] Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005; 67:2089-97.
- Goddard J, Turner AN, Stewart LH. Kidney and urinary tract disease. In: Colledge NR, Walker BR, Ralston SH

- (eds.) Davidson's principles and practice of Medicine, 20th ed. Edinburg: Churchill Livingstone; 2010. p. 487-8.
- 4. Coresh J, Astor BC, Greene T, et al. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis. 2003; 41: 1-12.
- **5.** Palmer BF. Sexual dysfunction in men and women with chronic kidney disease and end-stage kidney disease. Adv Ren Replace Ther. 2003; 10(1): 48-60.
- **6.** Finkelstein FO, Shirani S, Wuerth D, et al. Therapy Insight: sexual dysfunction in patients with chronic kidney disease. Nat Clin Pract Nephrol. 2007; 3: 200-7.
- 7. Leu TF. Erectile Dysfunction. N Eng J Med. 2000; 342: 1802-13.
- **8.** Roses SE, Joffe M, Franklin E, et al. Prevalence and determinants of ED in hemodialysis patients. Kidney Int. 2001; 59: 2259-66.
- **9.** Turk S, Karallezlib E, Yildiz M, et al. Erectile Dysfunction and the effects of sildenafil treatment in patients of hemodialysis and continuous ambulatory peritoneal dialysis. Nephro Dial Transplant. 2001; 6:1818-22.
- **10.** Kevin T, Vary M. Alteration in the sexual function. In: Fauci AS, Braunwald E, Kasper DL, et al. Harrisons principles of internal medicine. 17th ed., Vol. 2, USA: McGraw Hill; 2008. p. 296-300.
- **11.** Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. JAMA. 1999; 281: 537-43.
- **12.** Fung MM, Bettencourt R, Barrett-Connor E. Heart disease risk factors predict erectile dysfunction 25 years later: the Rancho Bernardo Study. J Am Coll Cardiol. 2004; 43: 1405-12
- **13.** Grover SA, Lowensteyn I, Kaouache M, et al. The prevalence of erectile dysfunction in the primary care setting: importance of risk factors for diabetes and vascular disease. Arch Intern Med. 2006; 166: 213-18.
- **14.** Sullivan ME, Keoghane SR, Miller MA. Vascular risk factors and erectile dysfunction. BJU Int. 2001; 87: 838-
- **15.** Greenstein A, Chen J, Miller H, et al. Does severity of ischemic coronary disease correlate with erectile function? Int J Impot Res. 1997; 9: 123-6.
- **16.** Chiurlia E, D'Amico R, Ratti C, et al. Subclinical coronary artery atherosclerosis in patients with erectile dysfunction. J Am Coll Cardiol. 2005; 46: 1503-11.
- **17.** Delano BG. Improvements in quality of life following treatment with r-HuEPO in anemic hemodialysis patients. Am J Kidney Dis. 1989; 14: 14-23.
- **18.** Palmer BF. Sexual dysfunction in uremia. J Am Soc Nephrol. 1999; 10: 1381-9.
- **19.** Ifudu O. Care of patients undergoing hemodialysis. N Engl J Med. 1998; 339: 1054-61.
- **20.** Grossman EB. The pharmacokinetics and hemodynamics of sildenafil citrate in male hemodialysis patients. Kidney Int. 2004; 66: 367-75.

- **21.** Rosen RC, Riley A, Wagner G, et al. The International Index of Erectile Function (IIEF): A multidimensional scale for assessment of erectile dysfunction. Urology. 1997; 49: 822-30.
- **22.** Rosen RC, Cappelleri J, Smith M, et al. Development and evaluation of an abridged, 5-item, version of the IIEF as a diagnostic tool for erectile dysfunction. Int J Impot Res. 1999; 11: 319-26.
- 23. Khan MH. Standardization and Validation of Urdu version of International Index of Erectile Function presented at first congress of world association of sexual health held at Sydney in April 15–19, 2007. Published in abstract book.
- **24.** Rosas SE, Jeffe M, Franklin E, et al. Association of decreased quality of life and erectile dysfunction in hemodialysis patients. Kidney Int. 2003; 64:232-8.
- **25.** Mehrsai S, Mousai M, Xthoobonkt T, et al. Improvement of erectile dysfunction KTP. Urology J. 2006; 3(4): 240-3.
- **26.** Inci K, Hazirolan T, Ati FT, et al. Coronary artery calcification in HD patients and their correlation with the prevalence of ED. Transplant Proc. 2008; 40(1): 77-80.
- **27.** Ali ME, Abdeel-Hafeez HZ, Mahran AM, et al. Erectile function in chronic renal failure patients undergoing hemodialysis in Egypt. Int J Impoten Res. 2005; 17(2): 180-7.
- **28.** Neto AF, freitac MA, Saraira Fitti JA et al. The epidemiology of ED and its correlation in men with chronic renal failure on hemodialysis in Londrina, Southern Brazil. Int J Impot Res. 2002; 14: 462-71.
- **29.** Miyata Y, Shindo K, Matsuya F, et al. Erectile dysfunction in hemodialysis patients with diabetes mellitus: association with age and haemoglobin a1c levels. Int J Urol. 2004; 11(7):530-6.
- **30.** Mersdorf A, Goldsmith PC, Diederichs W et al. Ultrastructural changes in impotent penile tissues. A comparison of 65 patients. J Urol. 1991; 145: 749-58.
- **31.** Cartledge JJ, Eardley L, Morrison JFB. Nitric oxide mediated corpus cavernous smooth muscle relaxation is impaired in ageing and diabetes. BJU Int. 2001; 87: 394-401.
- **32.** Klein R, Lee KB, Moss SE, et al. Prevalence of self reported erectile dysfunction in people with long term Insulin Dependent Diabetes Mellitus. Diab Care 1996; 19: 135-41.
- **33.** Rodger RS, Fletcher K, Dewar JH, et al. Prevalence and pathogenesis of impotence in one hundred uremic men. Uremia Invest. 1985; 8: 89-96.
- **34.** Chun Fu Lia, Wamg YT, Hung KU, et al. Sexual Dysfunction in peritoneal dialysis patients. Am J Nephrol. 2007; 27(6): 615-21.
- **35.** Rosas SE, Peng US, Yihron RL, et al. Prevalence and determinants of erectile dysfunction in hemodialysis patients. Kidney Int. 2001; 59: 2259-66.

- **36.** Arslan D, Aslan G, Sifil A, et al. Sexual dysfunction in male patients on hemodialysis: assessment with the International Index of Erectile Function (IIEF). Int J Impot Res. 2002; 14: 539-42.
- **37.** Kohler TS, Feia JK, Bodie J, et al. Prevalence of androgen deficiency in men with erectile dysfunction. Urology. 2008; 71(4): 693-9.
- **38.** Rosas SE. Prevalence and determinants of erectile dysfunction in hemodialysis patients. Kidney Int. 2001; 59: 2259-66.
- **39.** Mumtaz A, Anees N, Barki MH, et al. Erectile dysfunction in haemodialysis patients. J Ayub Med Coll Abbottabad. 2009; 21(2): 621-9.
- **40.** Eardley L. Effect of ageing and diabetes on smooth muscle relaxation. BJU Int. 2004; 117: 782-88.

- **41.** Steele TE, Wuerth D, Finkelstein S, et al. Sexual experience of the chronic peritoneal dialysis patients. J Am Soc Nephrol. 1996; 7: 1165-8.
- **42.** Messina LE, Claro JR, Nardozza A, et al. Erectile dysfunction in patients with chronic renal failure. Int Braz J Urol. 2007; 33: 673-8.
- **43.** Malekman L, Shakeri S, Haghpanah S, et al. Epidemiology of erectile dysfunction in haemodialysis patients using IIEF Questionnaire. Saudi J kidney Dis Transpl. 2011; 22(2): 232-37.

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E-mail: <u>dr_arif31@yahoo.com</u> Received: 6th Nov. 2013: Accepted 3rd Sep. 2014.