Sexual Dysfunction in Nondiabetic Hemodialysis Patients

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ABSTRACT

Background: *Erectile Dysfunction (ED) is a distressing problem in Chronic Renal Failure (CRF) and Hemodialysis (HD) patients and could be attributed to anemia which worsens the general condition and aggravates asthenia.* **Aim of the works:** *Detection of the prevalence of Erectile Dysfunction (ED) in Chronic Renal Patients (CRF) on Hemodialysis (HD).* **Patients and methods:** *50 patients on HD were assessed using IIEF-5 score, hormonal assay for Luteinizing Hormone (LH), prolactin and testosterone (total and free) and penile duplex study.* **Results:** *ED has very wide prevalence in CRF patients on HD with variable changes in levels of hormones and in duplex results.* **Conclusion:** *Prevalence of ED in CRF patients on HD is about 100% with variable degrees from mild to severe with changes in associated hormonal levels and results of duplex study.*

Keywords: Erectile dysfunction, Chronic renal failure, Non-diabetic, Hemodialysis

INTRODUCTION

Erectile Dysfunction (ED) is defined as the consistent inability to obtain or maintain erection for satisfactory sexual intercourse. It is well known that ED is a distressing problem in Chronic Renal Failure (CRF) and hemodialysis (HD) patients [1]. The prevalence of ED ranges between 21 and 43% among dialysis and this prevalence has remained the same since the 1970s [2]. ED could be attributed to anemia which worsens the general condition and aggravates asthenia in those patients especially when associated with hypoxia leading to decreased activity of Nitric Oxide (NO) bioavailability and increase in collagen synthesis [3]. The NO decrease also may be caused by reductions in the enzyme endothelial NO synthase (eNOS); Lack of substrate or cofactors for eNOS; Alterations in intracellular signaling such that eNOS is not appropriately activated or uncoupled; or accelerated degradation of NO by Reactive Oxygen Species (ROS), such as super oxide anion. All these factors well contribute to endothelial dysfunction which is referred to decreases in endothelium-dependent smooth muscle relaxation [4]. It is proved that the vascular endothelium can regulate vascular tone in the circulation by releasing a variety of factors that affect the contractile and relaxatory behavior of the underlying vascular smooth muscle together with playing a pivotal role in regulation of inflammation, platelet aggregation, vascular smooth muscle proliferation, and thrombosis [5]. From another point of view, hypercholesterolemia is one of the significant risk factors in uremic patients resulting in neurologic, arteriogenic, veno-occlusive, or cavernosal impairments with subsequent vasculogenic ED [6].

PATIENTS AND METHODS

This study included 50 male CRF patients on regular HD thrice weekly, have alive spouses and able to perform intercourse. Patients were subjected to the following: (1) History taking (age, smoking, sexual and medical history, dialysis duration). (2) Clinical examination including: General examination: with emphasis on manifestations of CRF and blood pressure measurement. Local genital examination: local examination of external genitalia to exclude congenital or acquired abnormalities, inspection of pubic area for hair distribution, localization of urethral orifice to exclude hypospadias, epispadias and phimosis. Size and development of testes, size of penis and presence of fibrosis, nodules indurations or peyronies plaque. Inclusion criteria: male, CRF controlled by HD. Exclusion criteria: Diabetic patients. (3) Evaluation of the erectile function assessed in the two categories, using the Arabic validated questionnaire of International Index of Erectile Dysfunction (IIEF-5) for classification of the severity of ED [7] was used. It classifies the severity of ED into five categories: No ED: IIEF erectile function domain scores 22-25, Mild ED: IIEF erectile, scores 17-21, moderately mild ED: II EF erectile function domain scores 12-16, Moderate ED: II EF erectile function domain scores 8-11 and Severe ED: II EF erectile function domain scores 5-7. All patients will be classified subsequently into: Normal erectile function and ED. Those with ED will be sub-classified into two categories: ED per se and ED with precipitating factor as hypertension, and cigarette smoking. (4) Estimating serum Luteinizing hormone (LH), Prolactin (PRL) and Testosterone (Test) (total and free).

(5) Penile duplex was performed. All statistical calculation was done using Computer Programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 16 for Microsoft Windows.
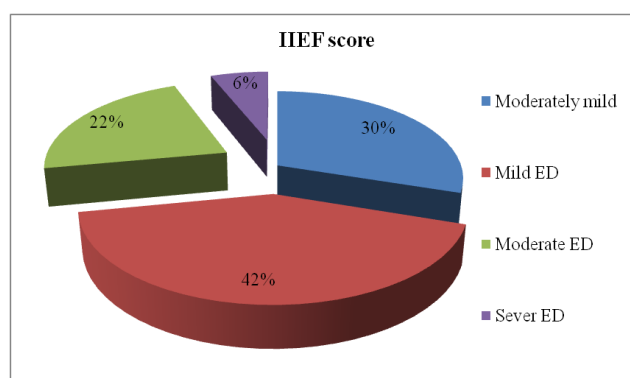
RESULTS

Between January 2016 to January 2017, 100 male patients with CRF on regular HD were screened and after 50 exclusions, 50 patients were randomly assigned to be included in the research with the following data (Tables 1-10; Figures 1-12).

Table 1: Descriptive analyses of age, IIEF score, LH, PRL, Test. (total and free), and dialysis duration

	N	Minimum	Maximum	Mean	SD
Age (year)	50	22	59	41.0	9.7
IIEF score	50	5	20	13.8	3.6
LH	50	1.1	9.4	3.3	2.2
PRL	50	2.3	23.8	15.0	8.4
Test (total)	50	1.49	10.8	4.6	2.7
Test (free)	50	1	8.9	3.6	2.4
Dialysis duration	50	12	84	41.4	20.9

Table 2: Percentage descriptive analyses of clinical findings

		Frequency	%
Smoking	No	13	26
	Yes	37	74
Duplex result	Normal	39	78
	Arteriogenic defect	11	22
Hypertension	Yes	50	100
	No	0	0
LH	Normal	49	98
	low	1	2
PRL	Normal	25	50
	High	25	50
Test. total	Normal	36	72
	Abnormal	14	28
Test. free	Normal	19	38
	Abnormal	31	62
IIEF score	Moderately mild	15	30
	Mild ED	21	42
	Moderate ED	11	22
	Sever ED	3	6

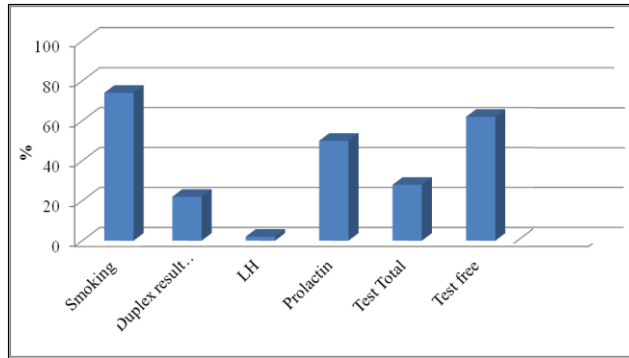**Figure 1: Percentage descriptive analyses of IIEF score**

Figure 2: Percentage descriptive analyses of smoking, duplex result, hypertension, LH, PRL, Test (total and free)

Table 3: Comparison between different IIEF scores according to age, LH, PRL, Test (total and free) and dialysis duration

	Moderately mild ED Mean ± SD	Mild ED Mean ± SD	Moderate ED Mean ± SD	Sever ED Mean ± SD	P-value	Sig.
Age	35.9 ± 8.2	42.8 ± 9.9	45.3 ± 9.2	37.3 ± 7.6	0.043	S
LH	3.5 ± 2.5	3.0 ± 1.8	2.8 ± 2.3	5.7 ± 3.0	0.212	NS
Prolactin	12.2 ± 8.7	16.1 ± 7.7	16.3 ± 8.7	16.6 ± 10.5	0.506	NS
Test(total)	5.6 ± 3.1	4.4 ± 2.6	4.2 ± 2.4	3.2 ± 1.6	0.372	NS
Test (free)	4.5 ± 2.7	3.3 ± 2.4	3.3 ± 1.9	2.4 ± 1.2	0.326	NS
HD duration	38.0 ± 24.0	43.2 ± 21.0	40.7 ± 14.5	48.0 ± 31.7	0.841	NS

The table show significant direct correlation between age and IIEF-5 score with P-value (0.043) and non-significant direct correlation with LH, PRL, Test. (total and free) or dialysis duration
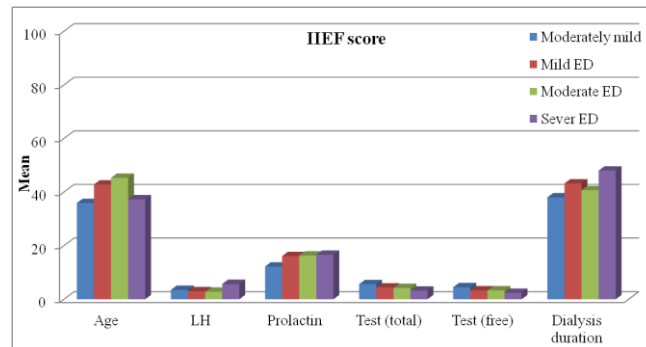

Figure 3: Comparison between Mean of different IIEF scores according to age, LH, PRL, Test (total and free) and dialysis duration

Table 4: Comparison between percentage of different IIEF scores according to smoking, duplex result, hypertension

	Moderately mild HD No. (%)	Mild ED No. (%)	Moderate ED No. (%)	Sever ED No. (%)	P-value	Sig.
Smoking	7 (46.7)	17 (81)	10 (90.9)	3 (100)	-0.031	S
Duplex result(Arteriogenic defect)	0 (0)	5 (23.8)	5 (45.5)	1 (33.3)	-0.049	S
Hypertension	15 (100)	21 (100)	11 (100)	3 (100)	1	NS

The table shows significant inverse correlation between smoking and IIEF-5 score with (P-value-0.031). Also there is significant inverse correlation between arteriogenic defect detected in duplex study and IIEF-5 score (P-value-0.049) and non-significant correlation between hypertension and IIEF-5 score
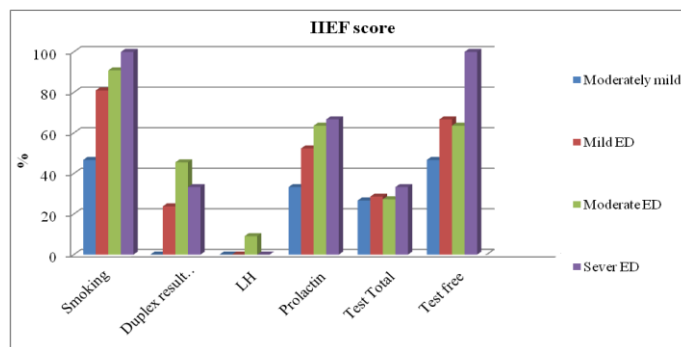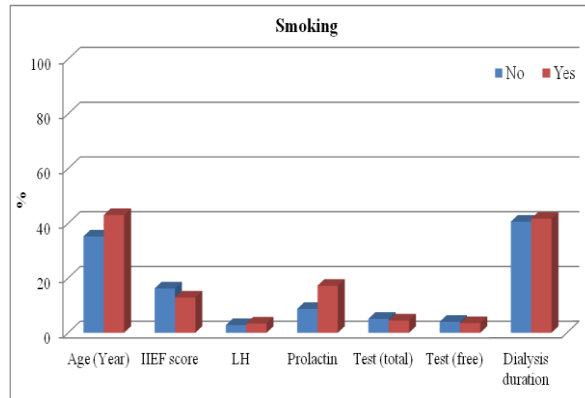

Figure 4: Comparison between percentage of different IIEF score according to smoking, duplex result, hypertension, LH, PRL, Test.(total and free)

Table 5: Comparison between no smoking and smoking patients according to age, IIEF score, LH, PRL, Test (total and free) and dialysis duration

	Smoking		P value	Sig.
	No (Mean ± SD)	Yes (Mean ± SD)		
IIEF score	16.2 ± 3.1	12.9 ± 3.5	-0.004	HS
LH	2.8 ± 1.2	3.4 ± 2.5	0.374	NS
Prolactin	8.7 ± 7.3	17.2 ± 7.6	0.001	HS
Test(total)	5.1 ± 3.0	4.5 ± 2.6	0.467	NS
Test(free)	4.0 ± 2.6	3.5 ± 2.3	0.456	NS
Dialysis duration	40.6 ± 22.7	41.7 ± 20.5	0.877	NS

The table shows highly significant inverse correlation between smoking and IIEF-5 score (P-value 0.004) also highly significant direct correlation between smoking and hyperprolactinemia (P-value 0.001)
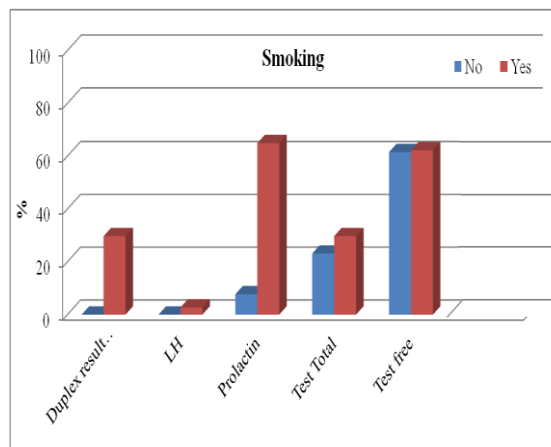

Figure 5: Comparison between no smoking and smoking patients according to age, IIEF score, LH, PRL, Test (total and free) and dialysis duration

Table 6: Comparison between percentage of no smoking and smoking patients according to duplex result, hypertension and IIEF score

		Smoking		P value	Sig.
		No (%)	Yes (%)		
Duplex result(Arteriogenic defect)		0(0)	11(29.7)	0.028	S
Hypertension		13(100)	37(100)	1	NS
IIEF score	Moderately mild	8(61.5)	7(18.9)	-0.004	HS
	Mild ED	4(30.8)	17(45.9)		
	Moderate ED	1(7.7)	10(27)		
	Sever ED	0(0)	3(8.1)		

The table shows significant direct correlation between smoking and arteriogenic defect detected in duplex study (P-value 0.028) and highly significant inverse correlation between smoking and IIEF-5 score (P-value 0.004).

Figure 6: Comparison between percentage of no smoking and smoking patients according to duplex result, hypertension, LH, PRL, Test (total and free)
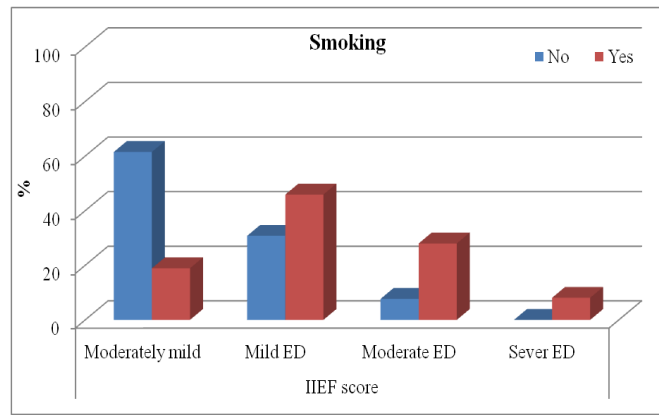
Figure 7: Comparison between percentage of no smoking and smoking patients according to different IIEF-5 scores

Table 7: Comparison between normal and arteriogenic defect (Duplex result) according to age, IIEF score, LH, PRL, Test (total and free) and dialysis duration

	Duplex result		P-value	Sig.
	Normal (Mean ± SD)	**Arteriogenic defect (Mean ± SD)**		
Age(Year)	37.5 ± 7.7	53.2 ± 4.5	0.001	HS
IIEF score	14.4 ± 3.7	11.5 ± 2.5	-0.015	S
LH	3.4 ± 2.5	2.7 ± 0.9	0.314	NS
PRL	14.8 ± 8.5	15.6 ± 8.1	0.785	NS
Test.(total)	4.3 ± 2.6	5.7 ± 2.9	0.135	NS
Test.(free)	3.4 ± 2.3	4.4 ± 2.6	0.236	NS
Dialysis duration	42.3 ± 21.9	38.1 ± 17.1	0.557	NS

The table shows highly significant direct correlation between arteriogenic defect detected in duplex study and age(P-value 0.001) and significant inverse correlation between arteriogenic defect and IIEF-5 score (P-value -0.015)

Table 8: Comparison between normal and arteriogenic defect (Duplex result) according to smoking, hypertension, LH, IIEF score

		Duplex result		P-value	Sig.
		Normal No. (%)	**Arteriogenic defect No. (%)**		
	Smoking	26(66.7)	11(100)	0.028	S
	Hypertension	39(100)	11(100)	1	NS
IIEF score	Moderately mild	15(38.5)	0(0)	0.007	HS
	Mild ED	16(41)	5(45.5)		
	Moderate ED	6(15.4)	5(45.5)		
	Sever ED	2(5.1)	1(9.1)		

The table shows significant direct correlation between arteriogenic defect detected in duplex study and smoking (P-value 0.028).
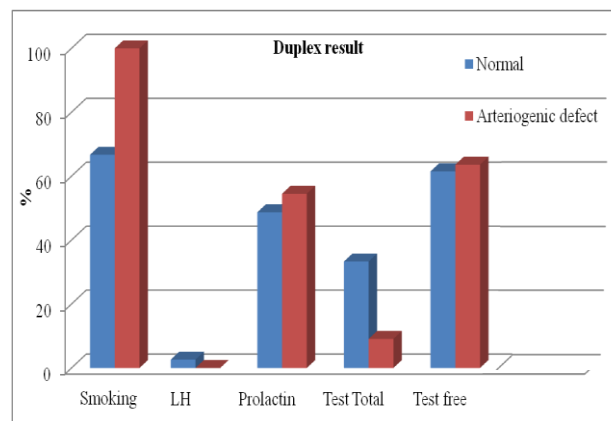

Figure 8: Comparison between normal and arteriogenic defect (Duplex result) according to smoking, hypertension, LH, PRL, Test(total and free)
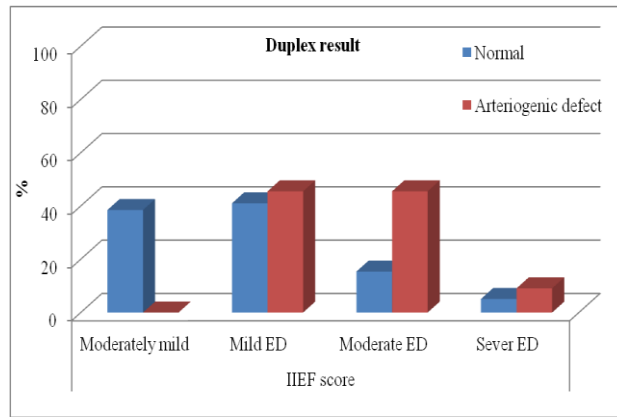
Figure 9: Comparison between normal and arteriogenic defect (Duplex result) according to different IIEF-5 scores

Table 9: Comparison between normal and high prolactin according to age, IIEF score, LH, Test (total and free) and dialysis duration

	Prolactin		P-value	Sig.
	Normal (Mean ± SD)	**High (Mean ± SD)**		
Ag e(Year)	38.3 ± 10.2	43.6 ± 8.5	0.042	S
IIEF score	14.4 ± 3.6	13.2 ± 3.7	0.233	NS
LH	2.8 ± 1.3	3.7 ± 2.8	0.160	NS
Test(total)	4.6 ± 2.6	4.7 ± 2.9	0.840	NS
Test(free)	3.6 ± 2.3	3.6 ± 2.5	0.979	NS
Dialysis duration	37.2 ± 21.9	45.6 ± 19.3	0.157	NS

The table shows significant direct correlation between hyperprolactinemia and age of patient (P-value 0.042).
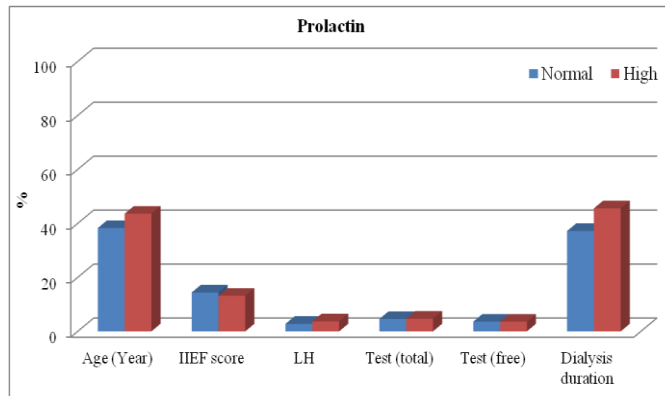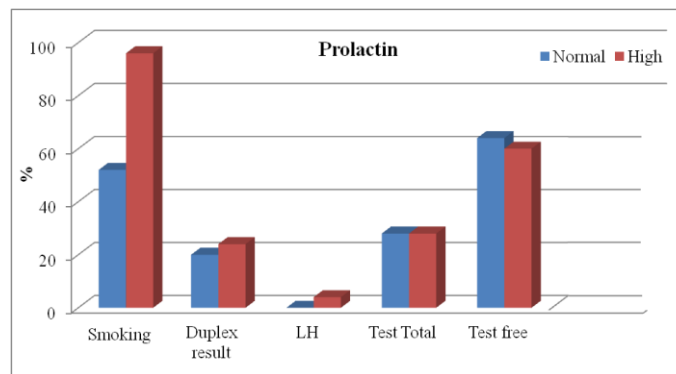

Figure 10: Comparison between normal and high prolactin according to age, IIEF score, LH, Test (total and free) and dialysis duration
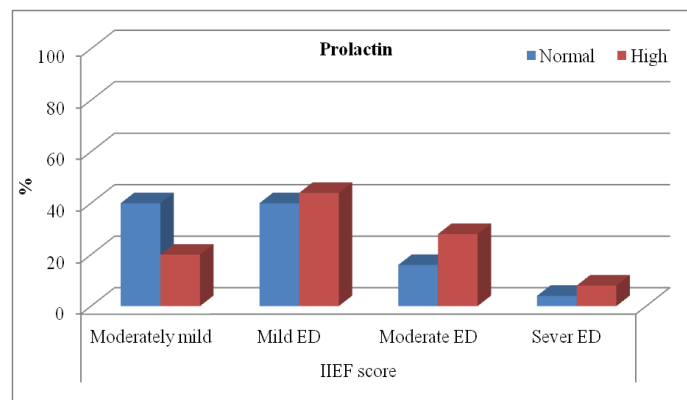
Table 10: Comparison between normal and high prolactin according to smoking, diabetes, duplex result, hypertension, IIEF score

		Prolactin		P-value	Sig.
		Normal No. (%)	**High No. (%)**		
	Smoking	13(52)	24(96)	0.001	HS
	Duplex result	5(20)	6(24)	0.735	NS
	Hypertension	25(100)	25(100)	1	NS
IIEF score	Moderately mild	10(40)	5(20)	0.097	NS
	Mild ED	10(40)	11(44)		
	Moderate ED	4(16)	7(28)		
	Sever ED	1(4)	2(8)		

The table shows highly significant direct correlation between increase PRL and smoking (P-value 0.001).

Figure 11: Comparison between normal and high prolactin according to smoking, diabetes, duplex result, hypertension, LH, Test (total and free)

Figure 12: Comparison between normal and high PRL according to IIEF-5 score

DISCUSSION

ED is defined by the National Institutes of Health (NIH) as the consistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance [8]. ED is estimated to be about 32% among the male population in the United States [9] and about 26% is Japan [10]. The estimated worldwide prevalence of ED in 1995 was 152 million, and it is forecast to increase to 322 million in 2025 [10]. In 2000, the Massachusetts Male aging study (MMAS) revealed that 52% of the whole population suffered from ED, and the prevalence increased with age from 38% in the youngest group to 70% in the oldest men. The presence of ED ranges between 21 and 43% among dialysis patients [10]. The prevalence of ED in Egypt estimated to be in those who had Moderate ED 10.3%, and those with complete ED were 13.2% [11]. In patients with chronic kidney disease (CKD), quality of life is poor due to the disease itself and its complications, such as Anemia, anorexia, stupor, decease cardiac response (congestive heart failure and muscle weakness) [12] CRF is a major health problem worldwide substantial due to disability symptoms, such as fatigue, lethargy, edema, legs itching, anorexia, headache, dizziness, shortness of breath and sleep Problems [13]. CRF has been associated with numerous disorders, such as auto-immune diseases including, diabetes mellitus, systemic lupus erythematous, mixed connective tissue disease, scleroderma, mixed cryoglubulinemia, Henoch-schonlinpurpura, vasculitis and others [14]. This study showed considerable negative association between age and ED in patients with CRF (P<0.043). Naya [15] had found that smoking was not a risk factor for ED within CRF patients. Our results supported this view as there was no significant Correlation was found between smoking in CRF patients and ED. Uremia affects local amino acids neurotransmitter outflow in hypothalamus, significantly affecting the release of Gonadotropin Releasing Hormones (GnRH) and hence affect Gn synthesis and secretion. In majority of patients, there is LHRH stimulation; the plasma LH level is elevated in HD patients. This increased level is due to prolonged half-life of LH as well as increased secretion of LH [16]. In our study, we found that 2% only of our patients had abnormal high level of LH with no significant correlation between LH level and IIEF-5 score (P-value 0.315). In our study, 50% of our patients had hyperprolactinemia with no significant correlation with IIEF-5 score (P-value 0.422). Androgen receptors are present in parasympathetic system and limbic system and thought to play an important role in erection. Uremic patients have lower serum testosterone levels. Testosterone binding capacity remains normal hence free testosterone level is also decreased [17]. Low testosterone is due to decreased production, increased metabolic and dialysis clearance and alteration in testosterone binding capacity but the normal circadian rhythm is still maintained [18]. In our study, 28% of our patients had low total testosterone level and 62% of our patients had low free testosterone level. We found non-significant correlation between total testosterone level and IIEF-5 score (P-value 0.996). Also no significant correlation between free testosterone level and IIEF-5 score (P-value 0.324). In our study, 22% of our patients had arteriogenic defect with indirect significant correlation with IIEF-5 score (P-value 0.049).

CONCLUSION

In our research we reported that the prevalence of ED in CRF patients on HD is about 100% with variable degrees from mild to severe with changes in associated hormonal levels and results of penile duplex study.

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