ORIGINAL ARTICLE

Course of Sexual Dysfunction in Different Domains among Hypertensive Patients: A Longitudinal Study in a Tier 2 City in India

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Abstract

Introduction: A greater risk of sexual dysfunction (SDys) is found in hypertensive individuals. The study aimed to chronicle the course of dysfunction in different domains of male and female sexual function in patients of essential hypertension and correlate the findings with different patient characteristics.

Materials and methods: The study was conducted in a semi-urban outpatient department setting, in Kolhapur city, consisting of 360 patients of essential hypertension on antihypertensive therapy for at least 2 years fulfilling the criteria of the study protocol in General medicine OPD of DY Patil Hospital and Research Institute. Detailed clinical history, examination, and laboratory investigations were carried out. Clinical data were collected using standard questionnaires. Demographics and clinical data were analyzed in R-studio software (v.1.2.5001).

Result: Of the 180 males, 46.11% ($n = 83$), and of 180 females, 38.89% ($n = 70$) had dysfunction in at least one domain. Among the 83 males with dysfunction, erectile dysfunction (Edys) was the commonest (100%) and lack of intercourse satisfaction (49%) was the least. Among the 70 females with dysfunction, lack of sexual desire was the commonest (78%) and lack of lubrication (46%) was the least. Age, antihypertensive drug type, and duration of antihypertensive treatment were significantly associated with dysfunction ($p < 0.005$). Sexual dysfunction improved in all the 25 males and 23 females who took treatment for it in the form of drugs and psychotherapy.

Conclusion: Sexual dysfunctions are more prevalent in hypertensive individuals. It should be aggressively screened, avoided, and treated since it is a sign of increased cardiovascular risk that also reduces the quality of life.

Keywords: Course, Hypertension, Sexual dysfunction.

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Introduction

Hypertension (HTN) is a leading risk factor for mortality mostly because of its high prevalence and associated risk of cardiovascular diseases.[1] Almost 25% of the world's adult population is estimated to have arterial hypertension by 2025. The estimated number is close to 1.5 billion.[2] Abnormalities of the vessels of our body, both structurally and functionally, are mainly associated with HTN. Long-term HTN causes blood vessel damage in general, the most frequent reason being vascular diseases.[3] Thus vessels in the genital region are also involved.[4] Reduced blood flow (secondary to hypertensive arteriosclerosis due to raised blood pressure) to the neural and systemic components of genitalia, subsequently leads to SDys.[5,6]

In addition, HTN treatment includes various classes of antihypertensive drugs, which could contribute to SDys due to their side effects.[7,8,4] Certain antihypertensive medications, especially diuretics and beta-blockers (β-blockers) may have undesirable effect on the sexual functioning.[9,10] So, SDys may be because of the natural progression of the disease itself and/or the antihypertensive medications.[9,11]

Sexual dysfunction is reported to be more prevalent when other cardiovascular risk factors coexist.[12] Hypertension in both males and females[13–15] has also been linked, with some reporting that HTN can cause decreased lubrication and dysfunction in orgasm in females.[14] Hypertension is also one of the most common comorbidities in people having problems with erection.[16–19]

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According to guidelines issued in 2013 by the European Society for Hypertension (ESH) and the European Society for Cardiology (ESC), there is a prevalence of hypertension in the general population of approximately 30–45%.[19] There is 44% female representation in Randomized Control Trial.[20] Also, early development of problems in erection can predict an asymptomatic cardiovascular disease.[20,21] It was recommended that SDys should be routinely evaluated in hypertensive women with a proper sexual history, and managed sensitively.[22] Hypertensive women are more

vulnerable to experience dysfunction, thus screening for it ought to be included in clinical care guidelines.[23]

Longitudinal data is sparse, and thus, a study to find out the impact of essential HTN in both genders is warranted. As an outcome of the research, we can find the prevalence of SDys in different domains. This data will be useful giving particular focus on that domain during routinely examining cases of HTN with SDys. Psychosexual counseling of hypertensive patients by focusing on that domain can be done to decrease problems due to improper fulfillment of sexual life. By following up with these patients, we will get a detailed knowledge of the effect of HTN and the effectiveness of therapy. This information can lay the foundation for future studies for studying the efficacy of individual antihypertensives on different domains.

Materials and Methods

In total, 180 males and 180 females were diagnosed with essential hypertension as per the new American College of Cardiology (ACC)/ American Heart Association (AHA) High Blood Pressure guidelines[24] and on antihypertensive therapy for at least 2 years, living with their partners, having no comorbidities that can cause SDys like diabetes mellitus, thyroid disorders, chronic liver disease (CLD) other than hypertension and having no history of cerebrovascular accident, trauma or surgery in the pelvic area, or any anatomical disorders of the genital tract and not taking psychotropic drugs regularly or not using any medication which could improve the desire or the level of sexual functioning (e.g., phosphodiesterase inhibitors, ayurvedic medications) coming to medicine OPD and for psychological counseling to the Psychiatry OPD of DY Patil Hospital and Research Institute were taken up for the study.

Patients with no history of thyroid disorders were examined for having hyperthyroidism according to Wayne's index of hyperthyroidism[25] and hypothyroidism according to Billewicz's diagnostic index.[26] Euthyroid patients, as per the scores, were taken up for the study. Patients who were not known case of CLD were examined for signs and symptoms of CLD as per Harrison's Principles of Internal Medicine (20th) edition. Those without such signs and symptoms were taken up. Informed written consent forms were given to the patients willing to participate in the study. For those giving consent to the study, semi-structured pro forma was used to obtain demographic data, and the socioeconomic class was assessed using Modified Kuppuswamy's scale.[27] The Female Sexual Function Index (FSFI)[28] and International Index of Erectile Function (IIEF) Questionnaires[29] were administered to hypertensive females and males respectively at the time of:

- First visit.
- Follow-up at 6 months.
- At the end of 12 months.

Both the questionnaires are standardized and validated having high sensitivity and specificity.[28,29] Female patients were interviewed in presence of a female attender. The findings from the first visit were correlated with patients' age, duration since antihypertensive therapy was initiated, and antihypertensive medications being taken by the patients. Treatment options for SDys were provided for those hypertensive patients who had SDys on OPD basis.

Patients those who opted to take treatment for SDys were given treatment as per Clinical Practice guidelines for the management of SDys.[30] The courses of SDys in patients who received treatment for SDys during the 1-year follow-up were compared to those who did not. During this period of 1 year, the patients starting antidiabetic, antithyroid drugs or those developing cerebrovascular accident, trauma, or surgery of the pelvic area were planned to be excluded from the study. Quantitative data were analyzed using *t*-test, Pearson's Correlation, Anova Scale, and Chi-square test of association. Data were analyzed using SPSSv23.0, i.e, Statistical Package for the Social Sciences software, and descriptive analysis was used.

Results

Table 1: Distribution of patients according to demographic variables

	Males		*Females*	
Categories	*Frequency (n)*	*Percentage (%)*	*Frequency (n)*	*Percentage (%)*
Age (years) ($n = 180$ each gender)				
<30	00	0.00	01	0.56
31–40	57	31.67	53	29.44
41–50	35	19.44	21	11.67
51–60	88	48.89	105	58.33
>60	00	0.00	00	0.00
Dysfunction in at least one domain ($n = 180$ each gender)	83	46.11	70	38.89
Socioeconomic level of patients with dysfunction in at least one domain (Males – $n = 83$; Females – $n = 70$)				
Lower	01	1.20	00	0.00
Lower middle	40	48.19	39	55.71
Upper	01	1.20	01	1.43
Upper lower	26	31.33	23	32.86
Upper middle	15	18.07	07	10.00

Table 2: Distribution of domains affected with age-group in males ($n = 180$)

	Age-group (in years)										
Domains affected	*<30*	*%*	*31–40*	*%*	*41–50*	*%*	*51–60*	*%*	*>60*	*%*	*Total*
AD	0	0.00	01	2.44	02	4.88	38	92.68	0	0.00	41
ED	0	0.00	04	28.57	06	42.86	04	28.57	0	0.00	14
ED, OD	0	0.00	01	100.00	00	0.00	00	0.00	0	0.00	01
ED, OD	0	0.00	01	20.00	01	20.00	03	60.00	0	0.00	05
ED, SD	0	0.00	00	0.00	00	0.00	10	100.00	0	0.00	10
ED, SD, OD, OS	0	0.00	04	33.33	01	8.33	07	58.33	0	0.00	12
Nil	0	0.00	46	47.42	25	25.77	26	26.80	0	0.00	97

p-value <0.0001, hence we found significant association; AD, dysfunction in all domains; ED, dysfunction in erectile dysfunction domain; Nil, no dysfunction in any domain; OD, orgasmic dysfunction; OS, dysfunction in overall satisfaction domain; SD, dysfunction in desire domain

Table 3: Distribution of domains affected in females with age-group

	Age-group (in years)										
Domains affected	*<30*	*%*	*31–40*	*%*	*41–50*	*%*	*51–60*	*%*	*>60*	*%*	*Total*
A, L, O, S, P	00	0.00	00	0.00	00	0.00	10	100.00	00	0.00	10
A, O, P	00	0.00	00	0.00	03	42.86	04	57.14	00	0.00	07
AD	00	0.00	00	0.00	04	23.53	13	76.47	00	0.00	17
D	00	0.00	06	28.57	01	4.76	14	66.67	00	0.00	21
D, A	00	0.00	11	100.00	00	0.00	00	0.00	00	0.00	11
D, A, L, O, S	00	0.00	00	0.00	00	0.00	05	100.00	00	0.00	05
D, A, S, P	00	0.00	00	0.00	00	0.00	01	100.00	00	0.00	01
Nil	01	0.93	36	33.33	13	12.04	58	53.70	00	0.00	108

p-value <0.0001, hence we found significant association; A, dysfunction in arousal domain; D, dysfunction in desire domain; L, dysfunction in lubrication domain; Nil, no dysfunction in any domain; O, dysfunction in orgasm domain; P, dysfunction in pain domain; S, dysfunction in satisfaction domain

Table 4: Distribution of domains affected with type of drug in males

	Type of drug						
Domain affected	*Beta blockers*	*%*	*CCB*	*%*	*T+H*	*%*	*Total*
AD	34	82.93	04	9.76	03	7.32	41
ED	05	35.71	06	42.86	03	21.43	14
ED, OD	01	100.00	00	0.00	00	0.00	1
ED, OD	04	80.00	00	0.00	01	20.00	5
ED, SD	04	40.00	00	0.00	06	60.00	10
ED, SD, OD, OS	11	91.67	01	8.33	00	0.00	12
Nil	35	36.08	34	35.05	28	28.87	97

p-value <0.0001, hence we found significant association

Table 5: Distribution of domains affected in females with type of drug

	Type of drug								
Domain affected	*Beta blockers*	*%*	*CCB*	*%*	*Diuretics*	*%*	*T+H*	*%*	*Total*
A, L, O, S, P	03	30.00	03	30.00	00	0.00	04	40.00	10
A, O, P	00	0.00	04	57.14	00	0.00	03	42.86	07
AD	08	47.06	05	29.41	00	0.00	04	23.53	17
D	05	23.81	05	23.81	00	0.00	11	52.38	21
D, A	08	72.73	01	9.09	00	0.00	02	18.18	11
D, A, L, O, S	04	80.00	01	20.00	00	0.00	00	0.00	05
D, A, S, P	01	100.00	00	0.00	00	0.00	00	0.00	01
Nil	45	41.67	32	29.63	03	2.78	28	25.93	108

p-value <0.0001, hence we found significant association. CCB, calcium channel blockers, T+H, thiazide plus Telmisartan combination

Table 6: Distribution of domains affected with duration since initiation of antihypertensive therapy in males

	Duration since initiation of antihypertensive therapy (in years)								
Domain affected	*<10*	*%*	*11–20*	*%*	*21–30*	*%*	*>30*	*%*	*Total*
AD	05	12.20	14	34.15	22	53.66	00	0.00	41
ED	06	42.86	07	50.00	01	7.14	00	0.00	14
ED, OD	00	0.00	06	100.00	00	0.00	00	0.00	06
ED, SD	03	30.00	07	70.00	00	0.00	00	0.00	10
ED, SD, OD, OS	03	25.00	09	75.00	00	0.00	00	0.00	12
Nil	76	78.35	20	20.62	01	1.03	00	0.00	97

p-value <0.0001, hence we found significant association

Discussion

Due to its high incidence and greater risk of causing cardiovascular diseases, long-term HTN can be fatal and should be addressed at the earliest.[1] More risk of developing SDys has been found in subjects with HTN.[15] When other cardiovascular risk factors combine, SDys might emerge as a possible adverse effect of treatment for HTN.[12] Hypertension has been linked to SDys in both genders, with some stating that HTN is associated with orgasmic dysfunction and reduced lubricative function in females.[13,14] Most of the studies done to date have mostly focused on the erectile function domain, with a handful of studies looking at the relationship between SDys in different domains in both genders and essential HTN. However, this area should be studied because sexual health is vital for an individual to lead a productive life. Therefore, the study is aimed to assess the course of SDys in different domains in patients with essential HTN and correlate the findings with different patient characteristics.

Sexual Dysfunction

Among the 83 males with SDys, EDys was the commonest dysfunction and was evident in all 83 males (100%), followed by low sexual desire (76%), orgasmic dysfunction (71%), lack of overall satisfaction (64%), and lack of intercourse satisfaction (49%) (Table 1). Contradictorily, The Treatment of Mild Hypertension Study (TOMHS), a first study that dealt with SDys in hypertensive patients, led to the belief that EDys has low prevalence rate of 12. 2% in men with dysfunction in any domain.[7] Those with hyperlipidemia, diabetes, older, or with moderate/severe HTN were excluded in TOMHS. However, at the conclusion, TOMHS reported highest frequency of EDys in the those under treatment for HTN or Systolic Blood Pressure (SBP) over 140 mm Hg.[7] Interestingly, diversified range of EDys prevalence was found in previous studies. Studies have reported variation in prevalence of EDys between 15 and 25% in the hypertensive patients.[31] Hypertension is a well-known risk factor for cardiovascular events and is extremely frequent in old age. Those with SBP >140 mm Hg are >twice as likely as men with SBP <140 mm Hg to have EDys. Importantly, pulse pressure (SBP minus diastolic BP), or a measure of arterial stiffness, is known to predict serious cardiovascular events in people with EDys.[31] Burchardt and workfellows assessed erectile functions in men having HTN aged 34–75 years with IIEF-5 and reported EDys in 68.3% among them.[32] A survey conducted by Giuliano et al. with 3906 hypertensive men (with no other comorbidities like diabetes), reported 67% cases of EDys.[33] However, this diversification can be due to the diagnostic method of EDys and sample characteristics.

Among the 70 females with SDys, loss of sexual desire was the commonest and was evident in 78% cases followed by lack of arousal (73%), orgasmic dysfunction (56%), pain (50%), lack of satisfaction (47%), and lack of lubrication (46%) (Table 1). These findings concur with a previous study by Nascimento et al., who too have reported high rates of SDys in women, with lack of desire (68.2%) being the commonest followed by lack of excitement (68.2%), lack of satisfaction (66.42%), pain (56.1%), lack of orgasm (55.4%), and lack of lubrication (41.1%).[34] Hypertension is a chronic vascular illness linked with structural or functional changes in target organs like the brain, heart, kidneys, and blood vessels, which might explain the high reported prevalence of SDys. Furthermore, the pathophysiology of SDys in HTN could be linked to nitric oxide (NO) and Phosphodiesterase-5, both of which have been found in the smooth muscle of the human clitoris, implying that NO plays a critical role in female sexual arousal, similar to erectile function. Chronic increase of SBP due to inadequate circulation reaching the genital tissue, which is crucial to sexual functioning, might result in FSD if the function of NO is reduced, as in essential HTN.[34] Additionally, increased BP causes blood vessel wall remodeling, resulting in poor blood flow to peripheral tissues.[4] Atherosclerosis-related genital blood flow reduction causes clitoral and vaginal vascular insufficiency, culminating in vasculogenic FSD.[35] Furthermore, reduced pelvic blood flow can cause fibrosis of the clitoral smooth muscle and the vaginal wall, limiting the normal sexual response.[36]

Age and SDys

The mean age for males is 48.67 years, and the median age is 52 years, and the mean age for females is 49.17 years, and the median age is 53 years (Table 2). The mean age of taking antihypertensive therapy was 9.56 years and 8.17 years.

A significant association was found between SDys and age in males. Sexual dysfunction in all domains were evident in the men aged 51–60 years (Table 3). However, a previous study conducted by Spatz et al. has also reported increased number of patients in higher age-group. Interestingly, they reported high number of patients aged 65–74 years.[37] Kinsey et al. also reported association between age and SDys in such patients.[38]

A significant association was observed between SDys and age in females. However, the age of 51–60 years is more prone to the SDys in all the domains (Tables 1 to 3).[4] This is reflected in this study as well. This can be attributed to the post-menopausal changes occurring in the body. Reduced estrogen levels in postmenopausal women can cause vaginal dryness, which can be exacerbated by inadequate pelvic blood flow, adversely impacting female sexual performance. Doumas et al. have reported that SDys rates gradually increases with age in hypertensive women (31–40 years, 21.2%; 41–50 years, 37.7%; 51–60 years, 56.8%).[4] Moreover, they have reported statistically significant differences between age-groups. Lunelli et al. also reported the correlation between age and SDys

among hypertensive women with mean age of 49.2 ± 9.2 years.[35] Surprisingly, in the present study, none of the SDys was reported by women above 60 years. This depicts that the women of this age-group were either unaware or ashamed of sharing such details.

Antihypertensive Drugs and SDys

In our study in both males and females with dysfunction, beta adrenergic blockers were significantly correlated with the same (Tables 4 and 5). Several commonly given antihypertensive medications, including methyldopa, diuretics, guanethidine, clonidine, and beta receptor blockers, have shown to induce or worsen sexual difficulties.[36–41] However, not all antihypertensive medications have the same risk of causing SDys,[42,43] certain drugs are linked with a higher prevalence of SDys than others.[44–47] Among the antihypertensive drug classes, beta blockers (β-blockers) are the most widely used. Furthermore, this is reflected in our study as a high number of patients were on β-blockers. The usage of first-generation β-blockers are reported to be associated with male SDys.[48] The second-generation Beta 1-selective blockers (atenolol) have lesser tendency to produce EDys than non-selective β-blockers. Contradictorily, Akinyede et al. illustrated that Calcium Channel Blockers (CCB) were the commonest cause of SDys, followed by angiotensin-converting enzyme inhibitors and diuretics.[49] In our study, no SDys was observed among patients taking diuretics only.

The role of the antihypertensive drug in SDys in women is still debatable due to contradictory results. Thomas et al., in their study, found no significant association between SDys and any antihypertensive drug class.[50] A previous study reported that β-blockers have adverse effect on SDys.[51] Contradictorily, Wassertheil-Smoller et al. and Perez-Stable et al. did not find any such adverse effect.[47,52]

Ogihara et al. reported that CCB and SDys are not associated.[53] Further, Grimm et al. also reported no significant association between ACE inhibitors, alpha-blockers, or thiazides and SDys. The findings of Spatz et al. too concur with other studies showing no significant association between Angiotensin-Converting Enzyme Inhibitors/Angiotensin II Receptor Blockers, CCB, diuretics, alpha, or β-blockers and female SDys.[53] However, this diversification in the results can be attributed to the study population and the way of validating sexual function.

Duration of Taking Antihypertensive Therapy and SDys

The prevalence of SDys among hypertensive patients was affected significantly by the duration of antihypertensive therapy. Among males, the dysfunction in all domains was observed in those taking anti-hypertensive therapy for 21–30 years and 11–20 years, with 22 (53.55%) and 14 (34.15%) cases, respectively (Table 6). Stunningly, despite several studies focusing on adverse impact of antihypertensives on sexual activities, there is paucity of studies that have focused on the link between the duration of antihypertensive therapy and SDys. Interestingly, Coward et al. studied the SDys in hypertensive patients treated with least common antihypertensive, losartan. They reported that 11.8% of the patients had improved sexual activity at the 12th week of treatment.[54] This discrepancy can be attributed to very less sample size and the duration of the study. However, this paucity in studies dealing with duration of antihypertensive therapy and SDys shed the light on the need for extensive study in the same area.

Among females, the dysfunction in all domains was observed in those taking treatment for <10 and 21–30 years with 11 (64.71%) and 6 (35.29%) number of cases, respectively. Tsiodras et al. illustrated that the duration of HTN has a substantial impact on the incidence/extent of SDys in women with HTN. Around 15.7% of women with essential HTN for <3 years had symptoms of SDys, but SDys was detected in 25 of 76 (32.9%) women with HTN for 3–6 years and 55 of 70 (78.6%) women with HTN for >6 years. They discovered a strong and substantial link between FSD and HTN duration as documented in the medical chart (p <0.001). Using partial correlation analysis, this relationship remained significant after adjusting for age.[4]

Treatment and Improvement in SDys

Of the 83 men with SDys, 25 opted for treatment. Of the 25, 48% were treated with the drug, while the other 52% were given drugs with non-pharmacological measures based on standard guidelines. Selection of treatment options was done on the basis of assessment as per standard guidelines.

Out of the 25, 16(64%) were put on Sildenafil. Out of them, 9 were on Sildenafil 50 mg daily and 7 were on Sildenafil 100 mg daily. Both groups took the medication 1 hour before intercourse and not more than one tablet/day. Out of 25, 9 (36%) were on Tadalafil 20 mg on alternate day regimen.

In total, 23 females with SDys took treatment, 4 were put on only drugs, and 19 were on drugs and non-pharmacological management combined. The selection of treatment options was done on the basis of assessment as per standard guidelines.

Out of 23, 14 were put on Bupropion in dosage of 300 mg/day (53%) and 9 were on Bupropion in dosage of 150 mg/day (47%).

During the treatment, significant association was found between SDys and age. Moreover, improvement was evident in all the patients. Dysfunction improved in all affected domains in those who took treatment for SDys. As the erectile function was mostly affected, improvement was maximum in that domain. This finding is concurrent with the previous studies that have dealt with the use of these drugs in treating SDys. Tadalafil is known, well-tolerated, safe and effective therapy for EDys of all severity and etiologies. Its effectiveness has been exemplified in multiple clinical trials. Besides being beneficial in the general EDys population, it is beneficial in difficult-to-treat EDys group with more severe EDys and more comorbidities too. Its extended half-life (17.5 hours) makes on-demand dosage possible; moreover, once-daily administration with effective steady-state plasma concentrations is also attainable. Tadalafil improves erectile function whether taken on-demand or once a day.[54]

Twenty-three to thirty percent males with EDys also have premature ejaculation (PE).[55,56] The American Urological Association advises treating the patient's EDys first, in men with both PE and EDys.[57] In fact, based on newly published evidence, European Urology Guidelines recommend[58] the use of PDE5 inhibitors in PE patients with/without EDys problems, either on its own or in conjunction with other treatments.[59–61] However, due to poor research design and a lack of acceptable outcomes in the published literature, the evidence on whether PDE5 inhibitors are beneficial in PE treatment is debatable.[62,63]

For the females, Bupropion was administered for treatment (300 mg per day/150 mg/day as per requirement). Sexual dysfunction improved in all affected domains in those who took treatment for SDys. As the desired domain was most affected, improvement was maximum in that domain. Modell et al. also

used Bupropion (300 mg per day/150 mg per day) and reported considerable progress with both doses of bupropion in overall satisfaction. However, they also reported significant satisfaction with orgasm intensity with the 150-mg/day dose. When they compared the sexual functioning of two doses, the difference was insignificant.[64]

Thus, to conclude, SDys in different in both genders are markedly prevalent in hypertensive individuals and significantly associated with age of the patients and duration of antihypertensive therapy. There was significant improvement in SDys following treatment also.

Our study has some limitations in the form of small sample size and questionable treatment compliance.

So, the study recommends clinicians to consider both pharmacological and non pharmacological management when deciding a treatment plan of patients with SDys. During the course of HTN, physicians should aggressively seek for symptoms of SDys for early intervention and better treatment compliance and management.

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