

## Clinical Prevalence and Associated Factors of Erectile Dysfunction in Patients Undergoing Haemodialysis

### Dear Editor,

Several studies among men with end-stage renal disease have estimated the prevalence of erectile dysfunction (ED) to range from 41.5% to 82%.<sup>1-3</sup> The aetiology of ED in men with chronic kidney disease (CKD) is multifactorial. As such, ED represents the sequel of the complex neuroendocrine and metabolic changes typical of uraemic syndrome.<sup>3,4</sup> In addition, pharmacological therapy for uraemia and the attendant physical and psychological stress may also play an important role in the genesis of this problem.<sup>5</sup>

This study aimed to assess the prevalence of sexual dysfunction, to identify the correlates of social, psychological, behavioural and metabolic factors, and to assess the extent of risk of comorbid cardiovascular and metabolic factors associated with the occurrence of ED in these male uraemic patients.

### Materials and Methods

This is a cross-sectional study based on data collected over a 3-year period—November 2011 to November 2014. A total of 1711 male renal patients were screened. Of this, 200 who had met the eligibility criteria of: i) age 21-65 years, and ii) undergoing haemodialysis therapy and clinical management at the National University Hospital, Singapore were recruited. All participants in this study were in stable relationships. Participants with cognitive deficiency and inability to communicate were excluded. Patients with chronic ambulatory peritoneal dialysis (CAPD) were also excluded to avoid other confounding factors for reporting of ED such as practical/physical constraints of CAPD and different baseline characteristics of CAPD patients.

Ethics approval for this questionnaire-based study was obtained from the National Healthcare Group Domain Specific Review Board (DSRB-ID-2011-00112) and all participants gave written informed consent. All participants completed 3 sets of questionnaires including a questionnaire concerning sociodemographic information, marital status, education, sexual intimacy, medical history, stress and lifestyle behaviour; the International Index of Erectile Function (IIEF) questionnaire; and the Patient Health Questionnaire (PHQ-9) which measures the severity of depression.

Coexisting medical conditions and duration on haemodialysis were ascertained from patients' medical

records. To enable meaningful analysis of relationship of ED with haemodialysis, the cutoff for aetiology of end-stage renal failure was  $\geq 90$  days in the present study. Of the original 200 subjects who were initially recruited for the study, 39 were excluded for the following reasons: i) duration of haemodialysis  $< 90$  days ( $n = 36$ ), and ii) incomplete answers on the questionnaire ( $n = 3$ ). Ultimately, 161 patients were included in the final analyses of this study.

Statistical analysis was performed using SPSS 21.0 PL for Windows. Multivariate logistic regression model was used to estimate odds ratio (OR), confidence interval (CI) of 95% for the relationship of ED with age, depression score, exercise, smoking, alcohol consumption and medical conditions in uraemia patients.  $P$  values  $< 0.05$  were considered statistically significant.

### Results

#### *Sociodemographic Characteristics*

The study sample was made up of 200 male patients, of whom 117 (58.5%) were Chinese, 55 (27.5%) were Malays and 21 (10.5%) were Indians. The age of participants ranged from 22 to 65 and mean  $\pm$  SD age was  $53.9 \pm 8.8$ . The majority of participants (45%) were between 51 and 60 years old. At the time of the survey, 189 participants (84.5%) were married and 102 (51%) had secondary school education.

#### *Prevalence of ED*

The prevalence for each of the 5 categories of ED is shown in Table 1. With IIEF cutoff score of 25 to define ED, the prevalence of ED of any degree was 93.3% (153/164) in this cohort. About 63% of uraemic subjects reported severe ED.

The comorbid cardiovascular and metabolic risk factors such as the prevalence of hypertension, diabetes mellitus

Table 1. Prevalence by Severity of Erectile Dysfunction

| Severity of ED | Severe (0 to 6) | Moderate (7 to 12) | Mild to Moderate (13 to 18) | Mild (19 to 24) | No ED (25 to 30) | Total |
|----------------|-----------------|--------------------|-----------------------------|-----------------|------------------|-------|
| Frequency      | 104             | 14                 | 17                          | 18              | 11               | 164   |
| Prevalence*    | 63.4            | 8.5                | 10.4                        | 11.0            | 6.7              | 100   |

ED: Erectile dysfunction

\*In percentage (%).

and hyperlipidaemia among the ethnic groups in Singapore are presented in Table 2. There was no significant association observed between the comorbid conditions and ethnic groups.

#### *Correlation of Severe ED Status with Other Factors*

As the proportion of ‘severe ED’ was quite high (63.4%), severe ED status was subsequently used as a binary variable to test for potential association with various factors including depression score, age, conditions (diseases), smoking, alcohol consumption, exercise frequency, and stress. The 2 minor ethnic groups—Indians ( $n = 18$ ) and Others ( $n = 2$ )—were merged for multivariate logistic regression analysis.

As shown in Table 3, 75.8% of cohort were aged  $\geq 50$  years. In view of the small number of young subjects, binarised age was used to explore the relationship of age with severe ED. Analysis based on binarised age ( $<50$  or  $\geq 50$ ) revealed a significant higher odds of having severe ED as age increased (OR: 5.81 with 95% CI: 2.27 to 14.88;  $P$  value  $<0.001$ ). Interestingly, among the ethnic groups, Malays had significantly lower odds of having severe ED (OR: 0.31 with 95% CI: 0.13 to 0.74;  $P$  value  $<0.008$ ).

About 54% of the subjects had diabetes which significantly increased odds of uraemic patients having severe ED (OR: 2.95 with 95% CI: 1.2 to 7.27;  $P$  value = 0.019). The overall prevalence of other comorbid cardiovascular problems, obesity, hyperlipidaemia and hypertension was 38.5%, 7.5%, 52.2% and 75.2% respectively. However, no significant association was observed between severe ED status and prevalence of these cardiovascular and metabolic conditions.

Severe ED status was also not associated with mean depression score (5.65 for severe ED group vs 4.95 for not severe ED group; OR: 1.02 with 95% CI: 0.95 to 1.1;  $P$  value = 0.600) or smoking and alcohol consumption. A significant association between exercise and severe ED status was observed when participants’ responses to the question on frequency of exercise in the recent 1 month (daily/once or twice a week/once or twice a month/never) was analysed. The trend was potentially U-shaped suggesting that those who exercise moderately (i.e. exercise once or twice a week) were least likely to have severe ED.

## **Discussion**

To the best of our knowledge, this study is the first to assess the prevalence, severity and clinical correlates of ED in male uraemia patients undergoing dialysis in Singapore. The incidence and severity of ED was notably high in the current study. Using IIEF as a tool to assess ED, 93.3% of men on haemodialysis reported ED, whereas 63.4% experienced severe ED. These values are considerably higher than those estimated from recent cohort studies ( $>100$  subjects) in Latin American and European countries (68.2% to 83% for ED and 43.0% to 47.0% for severe ED).<sup>6,7</sup> The higher prevalence of ED in the current study may be accountable by the higher rate of diabetes (54%)—which is an established independent risk factor of ED—as compared to 18.4% and 25.1% in the study population undertaken by Costa et al<sup>6</sup> and Vecchio et al<sup>7</sup> respectively. Another aggravating factor could possibly be that the proportion of participants in this study aged above 50 (75.8%) was considerably higher than that of the cohort in the study by Vecchio and colleagues (63%).<sup>7</sup> The differences in reported prevalence rates of ED between different studies had been attributable to age, study populations, and type of study tool used to assess the presence of ED.<sup>8</sup>

In clinical setting, the low incidence of ED in Malays may be due to some Malays quitting smoking. Due to data size restriction in the present study, the true incidence of ED in Malay haemodialysis patients awaits further confirmation in a larger patient cohort.

Consistent with previous studies on male haemodialysis patients, our multivariate regression analysis revealed that age ( $>50$ ) and diabetes are key correlates to severe ED in uraemia.<sup>2,9</sup> Based on our data, the incidence of ED in men with haemodialysis is almost twofold of that in the general population.<sup>10</sup> The lack of significance of important comorbid risk factors may be related to the extremely high prevalence of ED in our cohort and our analysis of cohorts with severe ED versus not severe ED—as opposed to extreme ends of the spectrum which might explain the lack of differentiation between the cohorts with regard to individual risk factors.

Table 2. Prevalence of Comorbid Cardiovascular and Metabolic Factors by Ethnicity

| Medical Condition |     | Chinese<br>n (%) | Malays<br>n (%) | Indians<br>n (%) | Others<br>n (%) | Total<br>n | P Value |
|-------------------|-----|------------------|-----------------|------------------|-----------------|------------|---------|
| Hypertension      | No  | 17 (41.5)        | 17 (41.5)       | 5 (12.2)         | 2 (4.9)         | 41         | 0.222   |
|                   | Yes | 74 (60.2)        | 36 (29.3)       | 13 (10.6)        | 0 (0)           | 123        |         |
| Diabetes          | No  | 45 (58.4)        | 24 (31.2)       | 7 (9.1)          | 1 (1.3)         | 77         | 0.864   |
|                   | Yes | 46 (52.9)        | 29 (33.3)       | 11 (12.6)        | 1 (1.1)         | 87         |         |
| Cardiovascular    | No  | 58 (56.9)        | 35 (34.3)       | 7 (6.9)          | 2 (2.0)         | 102        | 0.756   |
|                   | Yes | 33 (53.2)        | 18 (29.0)       | 11 (17.7)        | 0 (0)           | 62         |         |
| High cholesterol  | No  | 42 (53.2)        | 26 (32.9)       | 10 (12.7)        | 1 (1.3)         | 79         | 0.919   |

Table 3. Multivariate Analysis Stratified by Age, Ethnicity, Lifestyle Risk Behaviour and Medical Condition in 161 Subjects With and Without Severe Erectile Dysfunction

| Type                           | Variable                      | Levels                    | n (%)             | Severe ED<br>n (%) | Not Severe<br>ED n (%) | Odds Ratio<br>(95% CI) | SE    | P<br>Value |
|--------------------------------|-------------------------------|---------------------------|-------------------|--------------------|------------------------|------------------------|-------|------------|
| Basic                          | Age<br>(binary)               | <50                       | 39 (24.2)         | 14 (35.9)          | 25 (64.1)              | 1 (reference)          |       |            |
|                                |                               | ≥50                       | 122 (75.8)        | 88 (72.1)          | 34 (27.9)              | 5.81 (2.27 to 14.88)   | 0.48  | <0.001     |
|                                | Ethnicity                     | 1 (Chinese)               | 89 (55.3)         | 66 (74.2)          | 23 (25.8)              | 1 (reference)          |       | 0.018*     |
|                                |                               | 2 (Malay)                 | 52 (32.3)         | 26 (50)            | 26 (50)                | 0.31 (0.13 to 0.74)    | 0.44  | 0.008      |
|                                |                               | 3 (Indian & Others)       | 20 (12.4)         | 10 (50)            | 10 (50)                | 0.38 (0.11 to 1.26)    | 0.61  | 0.114      |
|                                | Depression score <sup>†</sup> |                           | 5.39 <sup>†</sup> | 5.65 <sup>†</sup>  | 4.95 <sup>†</sup>      | 1.02 (0.95 to 1.1)     | 0.04  | 0.600      |
|                                | Exercise<br>frequency         | 1 (daily)                 | 35 (21.7)         | 22 (62.9)          | 13 (37.1)              | 1 (reference)          |       | 0.045*     |
|                                |                               | 2 (once or twice a week)  | 33 (20.5)         | 13 (39.4)          | 20 (60.6)              | 0.43 (0.14 to 1.37)    | 0.59  | 0.153      |
|                                |                               | 3 (once or twice a month) | 18 (11.2)         | 11 (61.1)          | 7 (38.9)               | 1.26 (0.32 to 5.05)    | 0.71  | 0.740      |
|                                |                               | 4 (never)                 | 75 (46.6)         | 56 (74.7)          | 19 (25.3)              | 1.87 (0.68 to 5.16)    | 0.52  | 0.224      |
| Lifestyle<br>risk<br>behaviour | Smoke                         | No                        | 136 (84.5)        | 85 (62.5)          | 51 (37.5)              | 1 (reference)          |       |            |
|                                |                               | Yes                       | 25 (15.5)         | 17 (68)            | 8 (32)                 | 1.06 (0.34 to 3.29)    | 0.58  | 0.916      |
|                                | Consume<br>alcohol            | No                        | 158 (98.1)        | 100 (63.3)         | 58 (36.7)              | 1 (reference)          |       |            |
|                                |                               | Yes                       | 3 (1.9)           | 2 (66.7)           | 1 (33.3)               | 0.7 (0.04 to 13.08)    | 1.49  | 0.814      |
| Medical<br>condition           | Diabetes                      | No                        | 74 (46.0)         | 39 (52.7)          | 35 (47.3)              | 1 (reference)          |       |            |
|                                |                               | Yes                       | 87 (54.0)         | 63 (72.4)          | 24 (27.6)              | 2.95 (1.2 to 7.27)     | 0.46  | 0.019      |
|                                | Obesity                       | No                        | 149 (92.5)        | 93 (62.4)          | 56 (37.6)              | 1 (reference)          |       |            |
|                                |                               | Yes                       | 12 (7.5)          | 9 (75)             | 3 (25)                 | 2.93 (0.56 to 15.22)   | 0.84  | 0.201      |
|                                | High<br>cholesterol           | No                        | 77 (47.8)         | 47 (61.0)          | 30 (39)                | 1 (reference)          |       |            |
|                                |                               | Yes                       | 84 (52.2)         | 55 (65.5)          | 29 (34.5)              | 0.77 (0.3 to 1.98)     | 0.48  | 0.583      |
|                                | Hypertension                  | No                        | 40 (24.8)         | 24 (60)            | 16 (40)                | 1 (reference)          |       |            |
|                                |                               | Yes                       | 121 (75.2)        | 78 (64.5)          | 43 (35.5)              | 0.81 (0.33 to 2.01)    | 0.46  | 0.648      |
| Cardiovascular                 | No                            | 99 (61.5)                 | 62 (62.6)         | 37 (37.4)          | 1 (reference)          |                        |       |            |
|                                | Yes                           | 62 (38.5)                 | 40 (64.5)         | 22 (35.5)          | 0.58 (0.24 to 1.38)    | 0.44                   | 0.216 |            |
| Total                          |                               |                           | 161               | 102                | 59                     |                        |       |            |

CI: Confidence interval; ED: Erectile dysfunction; SE: Standard error

\*Overall *P* value of the corresponding predictor.

†Mean score.

The increased incidence of ED in haemodialysis patients may be caused by vascular diseases (endothelial dysfunction, arteriosclerosis), neuroendocrine and metabolic changes including lower testosterone levels, suppression of the pituitary testicular axis, hyperprolactinaemia, hyperthyroidism and zinc deficiency.<sup>11,12</sup> Chronic fatigue and anxiety (e.g. financial strain of the disease) which are prevalent in patients undergoing dialysis may lead to lack of sexual desire and decline in frequency of sexual activity. In addition, fear that sex may worsen the condition may further negatively impact on the frequency of intercourse.

It has been estimated that about 20% to 30% of dialysis patients are depressed at any one time.<sup>12</sup> However, the present study did not find any significant association between depression and severe ED even though the presence of depressive symptoms has been identified as an independent factor of sexual dysfunction in male

haemodialysis patients.<sup>7,9,13</sup> Failure to detect significant association between depression and severe ED may be due to cross-sectional design or limitations in the instrument/questions used to assess depression.

A limitation of this study is that administration of medication known to be causally associated with ED such as beta blockers, thiazide diuretics, tricyclic antidepressants, and selective serotonin reuptake inhibitors have not been ruled out.<sup>14,15</sup> This study also did not evaluate metabolic factors such as dialysis adequacy, albumin and parathyroid hormone levels which may have played a part in the prevalence of ED in male patients undergoing haemodialysis.<sup>7</sup>

## Conclusion

Our cross-sectional study reveals that 63.4% of uraemia patients experienced severe ED. Both diabetes and ageing

were significantly associated with severe ED. These observations reinforce the importance of prophylactic and/or management options for improvement of reproductive/sexual health-related quality of life for men with uraemia and their partners.

#### Acknowledgement

*This work was supported by the National Kidney Foundation Singapore – Venerable Yen Pei Research Fund (NKFRC/2010/07/15).*

#### REFERENCES

- Palmer BF. Sexual dysfunction in uremia. *J Am Soc Nephrol* 1999;10:1381-8.
- Rosas SE, Joffe M, Franklin E, Strom BL, Kotzker W, Brensinger C, et al. Prevalence and determinants of erectile dysfunction in hemodialysis patients. *Kidney Int* 2001;59:2259-66.
- Nassir A. Sexual function in male patients undergoing treatment for renal failure: a prospective view. *J Sex Med* 2009;6:3407-14.
- Bellinghieri G, Santoro D, Mallamace A, Savica V. Sexual dysfunction in chronic renal failure. *J Nephrol* 2008;21 Suppl 13:S113-7.
- Lew-Starowicz M, Gellert R. The sexuality and quality of life of hemodialyzed patients – ASED multicenter study. *J Sex Med* 2009;6:1062-71.
- Costa MR, Reis AM, Pereira BP, Ponciano VC, Oliveira EC. Associated factors and prevalence of erectile dysfunction in hemodialysis patients. *Int Braz J Urol* 2014;40:44-55.
- Vecchio M, Palmer S, De Berardis G, Craig J, Johnson D, Pellegrini F, et al. Prevalence and correlates of erectile dysfunction in men on chronic haemodialysis: a multinational cross-sectional study. *Nephrol Dial Transplant* 2012;27:2479-88.
- Navaneethan SD, Vecchio M, Johnson DW, Saglimbene V, Graziano G, Pellegrini F, et al. Prevalence and correlates of self-reported sexual dysfunction in CKD: a meta-analysis of observational studies. *Am J Kidney Dis* 2010;56:670-85.
- Peng YS, Chiang CK, Hung KY, Chiang SS, Lu CS, Yang CS, et al. The association of higher depressive symptoms and sexual dysfunction in male haemodialysis patients. *Nephrol Dial Transplant* 2007;22:857-61.
- Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol* 1994;151:54-61.
- Kaufman JM, Hatzichristou DG, Mulhall JP, Fitch WP, Goldstein I. Impotence and chronic renal failure: a study of the hemodynamic pathophysiology. *J Urol* 1994;151:612-8.
- Suzuki E, Nishimatsu H, Oba S, Takahashi M, Homma Y. Chronic kidney disease and erectile dysfunction. *World J Nephrol* 2014;3:220-9.
- Park HC, Yoon HB, Son MJ, Jung ES, Joo KW, Chin HJ, et al. Depression and health-related quality of life in maintenance hemodialysis patients. *Clin Nephrol* 2010;73:374-80.
- Chrysant SG. Antihypertensive therapy causes erectile dysfunction. *Curr Opin Cardiol* 2015;30:383-90.
- Kennedy SH, Rizvi S. Sexual dysfunction, depression, and the impact of antidepressants. *J Clin Psychopharmacol* 2009;29:157-64.

Lang Chu Lau, <sup>1</sup>MSc, P Ganesan Adaikan, <sup>1</sup>PhD, DSc,  
Anantharaman Vathsala, <sup>2</sup>MD, FRCP, FAMS,  
Balasubramanian Srilatha, <sup>1</sup>MD, PhD,  
Mee Lian Wong, <sup>3</sup>MBBS, MPH, MD, Chuen Seng Tan, <sup>3</sup>PhD,  
Xiaodong Deng, <sup>3</sup>MSc, Hersharan Kaur Sran, <sup>2</sup>MBBS,  
Lee Hwee Koh, <sup>2</sup>BSc(Hons), Valerie Ma, <sup>2</sup>SRN

<sup>1</sup>Department of Obstetrics & Gynaecology, National University Hospital, Singapore

<sup>2</sup>Division of Nephrology, Department of Medicine, National University Hospital, Singapore

<sup>3</sup>Saw Swee Hock School of Public Health, National University Health System, National University of Singapore, Singapore

Address for Correspondence: Prof P Ganesan Adaikan, Department of Obstetrics & Gynaecology, National University Hospital, NUHS Tower Block, Level 12, 1E Kent Ridge Road, Singapore 119228.  
Email: obgadaik@nus.edu.sg