Prevalence and determinants of Anxiety and Depression in End Stage Renal Disease (ESRD). A comparison between ESRD patients with and without coexisting Diabetes Mellitus

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Abstract

OBJECTIVE:

To compare anxiety and/or depressive symptoms between patients with end-stage renal disease with and without comorbid diabetes and identify factors associated with symptoms of distress in this population

METHODS:

Data from two studies (conducted between 2010 - 2014) were pooled. A total of 526 patients on hemodialysis (68.8% with diabetes) completed the Hospital Anxiety and Depression Scale (HADS). Elevated symptoms were defined as HADS-Anxiety or HADS-Depression ≥8. Univariate and multivariate logistic regressions were used to estimate associations between diabetic status, and other socio-demographic and clinical factors with baseline clinical anxiety and depression.

RESULTS:

A total of 233 (45.4%) reported elevated anxiety symptoms and 256 (49.9%) reported elevated depressive symptoms sufficient for caseness. Rates were not different between patients with and without diabetes. Risk for clinical depression was higher in patients who were single/unpartnered (OR = 1.828), Chinese vs. Malay (OR = 2.05), or had lower albumin levels (OR = 0.932). None of the parameters were associated with anxiety caseness.

CONCLUSION:

Sociocultural factors rather than comorbid burden may help identify patients at risk for depression. The high rates of anxiety and depression underlie the importance for monitoring and intervention in dialysis care.

Keywords: Anxiety, Depression, Diabetes mellitus, End-stage renal disease

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Emotional distress, as indexed by symptoms of anxiety and depression, is common in chronic illness. Incidence/prevalence rates and severity of symptoms are markedly higher in patients with long term conditions, e.g. diabetes mellitus (DM) [1], heart disease [2], rheumatoid arthritis [3] or chronic kidney disease [4], compared to the general population. While exact estimates may vary due to methodological/measurement differences across studies, there is overwhelming evidence that chronic illness with comorbid depression is associated with increased symptom burden and functional impairment, poor quality of life, non-adherence to treatment, and worse clinical outcomes [5,6].

Multimorbidity, the co-occurrence of two or more physical conditions that require active management, can intensify treatment demands and psychological impact over and beyond that of individual conditions [7]. In particular, end-stage renal disease (ESRD) with comorbid diabetes has emerged as a new challenge for health services. Over 50% of dialysis patients receive renal replacement therapy due to diabetic nephropathy [8,9]. They represent the fastest growing and most 'frail' patient segment in renal care worldwide. The greater comorbid burden and treatment demands/complexity for DM ESRD patients [10] could aggravate symptoms of distress [11] and hinder emotional adjustment. Yet, while DM ESRD patients are known to have poorer prognoses, little is known on the psychological status of this group relative to general ESRD population [12]. There is clear need to evaluate these outcomes to develop efforts to provide better care.

The present study aimed to document and compare prevalence rates of anxiety and depression between ESRD patients with and without coexisting DM, hypothesizing that DM patients would experience greater psychological distress given greater comorbid burden, as

well as identify other socio-demographic and clinical factors associated with anxiety and depression in the ESRD population.

Methods

Data used were pooled from two studies, conducted between 2009 [13] and 2014 [14] in National Kidney Foundation (NKF), Singapore. These included baseline data (collected prior randomization) from the HED-SMART trial, a pragmatic RCT (Trial Registration: ISRTN31434033) to evaluate the effectiveness of self-management intervention to improve clinical and patient reported outcomes in hemodialysis patients (13) and data from a Phase I study (CDIRECT – Combined Diabetes and Renal Control Trial) undertaken to examine needs of patients with coexisting diabetes (either Type 1 or Type 2) and ESRD so as to develop a specific program of support [14]. Study protocols were in compliance with the Helinski declaration and were approved by the NUS Institutional Review Board. Eligible participants were recruited from the general pool of patients in the dialysis centres by research personnel independent to their renal care team. Inclusion criteria for both studies were: (i) age ≥21 years, (ii) on hemodialysis for a minimum of 3 months, (iii) able to understand English and/or Mandarin or Malay, and (iv) free of cognitive, major visual or auditory impairments and life-limiting condition diagnosis (e.g. terminal cancer) as recorded in medical notes and verified by nurse manager in participating dialysis centres. Informed consent was obtained from all study participants.

Measures

Demographic information included gender, age, ethnicity, education, employment, marital/relationship status, monthly household income, living arrangement, and housing.

Medical records were reviewed to extract information on primary kidney diagnosis, months on dialysis, and measures of potassium, phosphate, haemoglobin, albumin and Kt/V. Comorbidity burden was assessed using the Charlson Comorbidity Index (CCI) [15].

The 14-item self-report Hospital Anxiety and Depression Scale (HADS) [16] was used to measure depressive and anxious symptoms (7 items each). Items are rated on a 4-point scale (0 to 3), with larger scores indicating greater severity of symptoms. The scale is widely used across patient populations and has been found to display reasonable sensitivity and specificity when caseness is defined by a score of 8 or higher for each subscale [17]. Either the English or Mandarin validated versions were used (as appropriate).

Statistical analyses

All statistical analyses were performed using SPSS V20. Continuous variables were expressed as means and standard deviations. Categorical variables were expressed as absolute values and percentages. Differences between ESRD subgroups in continuous variables were tested using independent sample t-tests, and differences in categorical variables were assessed using Pearson's χ^2 test. HADS-A and HADS-D scores were calculated and coded for caseness using the cut-off score of 8.

Univariate logistic regressions were conducted to investigate factors associated with anxiety and depression caseness. All parameters significant at univariate analyses were subsequently modelled in a multiple regression model. Percentage of variance explained was determined using Cox and Snell's R^2.

Results

The sample comprised 526 hemodialysis participants (Mean age: 56.1±10.8; 41.3% female; 53.8% Chinese) (Table I). Of these, 363 (68.8%) had diabetes, while the remaining 161 (30.9%) did not. Medical information was missing for the remaining 2 participants (0.3%). Mean HADS-A score (7.29±4.17) and HADS-D scores (7.82±4.24) were below the cut-off, hence considered to be in 'normal' range. Prevalence of caseness for anxiety and depression based on the cut-off was 45.2% and 50.4% respectively.

Significant casemix differences between DM ESRD and non-DM ESRD were noted on several socio-demographic parameters (Table I). Patients with DM ESRD were older, had lower education and employment rates and were less likely to be home owners or Chinese. They had been on dialysis for a shorter time (p<.001), had higher CCI scores (p<.001), higher albumin (p=.008) and lower haemoglobin levels (p<.001) compared to non-DM ESRD counterparts.

Comparisons indicated that depression levels were equivalent between DM ESRD (7.88±4.37) and non-DM ESRD patients (7.64±3.88). Anxiety levels were significantly higher in DM ESRD (7.66±4.09) relative to non-DM ESRD (6.41±4.18) (p =.001), though mean scores were still within normal ranges. Rates of anxiety (47.4% vs. 40.4%, p=.137) and depression (49.9% vs. 51.6%, p=.721) caseness were similar between DM ESRD vs. non-DM ESRD patients respectively. These effects persisted even after comparisons were adjusted for casemix differences, i.e. severity of symptoms of depression and rates of caseness for anxiety and depression remained equivalent across groups.

Table I

Summary comparison of demographic variables and clinical parameters

	Total	**Non-DM**	**DM**	
	M ± SD/*N (%)*	M ± SD/*N* (%)	M ± SD/*N* (%)	*p*
Total	526	161 (31)	363 (69)	-
HADS-Anxiety	7.28±4.153	6.41±4.184	7.66±4.086	.001**
Anxiety caseness (HADS≥8)	233 (45.4)	65 (40.4)	172 (47.4)	.137
HADS-Depression	7.81±4.225	7.64±3.879	7.88±4.373	.547
Depression caseness (HADS≥8)	256 (49.9)	83 (51.6)	181 (49.9)	.721
Socio-demographic variables				
Gender				.306
Male	309 (59)	89 (55)	218 (60)	
Female	217 (41)	72 (45)	145 (40)	
Age	56.10±10.84	51.45±11.84	58.10±9.67	<.001***
Ethnicity				.043*
Chinese	272 (53)	99 (62)	182 (50)	
Malay	185 (36)	48 (30)	138 (38)	
Others	55 (11)	13 (8)	43 (12)	
Relationship status				.340
With partner	340 (65)	109 (68)	231 (64)	
Without partner	184 (35)	51 (32)	131 (36)	
Highest Qualification Level				.003**
Primary and below	209 (40)	51 (32)	157 (44)	
Secondary	232 (45)	73 (46)	159 (44)	
Tertiary	80 (15)	36 (22)	43 (12)	
Employment status				<.001***
Employed/Student	143 (28)	72 (46)	71 (20)	
Unemployed	126 (24)	29 (19)	97 (27)	
Retired	98 (19)	17 (11)	80 (22)	
Looking after home and family	78 (15)	24 (15)	54 (15)	
Others	75 (14)	16 (10)	59 (16)	
Monthly Household Income				.716
$0 - $2000	257 (49)	81 (51)	174 (48)	
$2001 - $4000	123 (24)	34 (22)	89 (25)	
$4001 - $6000	23 (5)	9 (6)	14 (4)	
$6001 and above	18 (3)	7 (4)	11 (3)	
Don’t know	74 (14)	19 (12)	54 (15)	
Do not wish to answer	27 (5)	8 (5)	19 (5)	

Living Arrangement				<.001***
Home owner	206 (39)	84 (53)	122 (34)	
Renting	202 (39)	24 (15)	177 (49)	
Others	115 (22)	50 (32)	64 (17)	
Housing				.225
1-2 room public housing	59 (11)	13 (8)	45 (12)	
3-4 room public housing	370 (71)	121 (76)	247 (69)	
5 room public housing and above	92 (18)	26 (16)	68 (19)	
Clinical Parameters				
Primary Kidney Diagnosis				<.001***
Diabetes	309 (63)	0 (0)	310 (89)	
Hypertension	25 (5)	18 (13)	7 (2)	
Glomerulonephritis	93 (19)	74 (51)	20 (6)	
Others	62 (13)	52 (36)	11 (3)	
Time on Dialysis (months)	52.9±53.2	75.4±63.4	43.0±44.6	<.001***
Charlson Comorbidity Index	6.78±3.00	3.75±1.68	8.09±2.44	<.001***
Potassium (mmol/l)	4.70±0.65	4.75±0.65	4.68±0.66	.314
Phosphate (mmol/l)	5.01±2.74	5.49±3.44	4.80±2.35	.009**
Haemoglobin (g/dl)	11.02±1.54	11.51±1.39	10.81±1.56	<.001***
Albumin (g/dl)	35.55±3.69	34.96±3.11	35.82±3.87	.016**
Kt/V	1.57±0.42	1.61±0.29	1.55±0.47	.122

* $p < .05$, ** $p < .01$, *** $p < .001$

Factors associated with anxiety and depression prevalence

Increased prevalence of anxiety not associated with any variable (Table II) hence multivariate analysis was not performed.

For depression, univariate analyses revealed that increased prevalence was associated with higher phosphate levels (OR=1.132, *p*=.050) and lower albumin levels (OR=0.944, *p*=.021), and strongly associated with being single, widowed or divorced (OR=1.858, *p*=.001). Chinese also reported significantly higher rates of depression compared to both Malay (OR=1.748, *p*=.003) and "Other" ethnicities (OR=1.894, *p*=.032).

The multiple regression model including ethnicity, relationship status, phosphate and albumin levels explained 6.1% of the variance. The results also indicate that increased prevalence of depression is independently associated with being single, widowed or divorced (OR=1.827, *p*=.002), being Chinese vs. Malay (OR=2.05, *p*=.004) and lower albumin levels (OR=0.932, *p*=.006).

Table II

Univariate and multivariate logistic regressions for anxiety and depression caseness (*n* = 526)

Variables	**Anxiety**				**Depression**						
	Univariate				Univariate				Multivariate		
	OR	95% CI	*p*	R^2	OR	95% CI	*p*	R^2	OR	95% CI	*p*
Diabetes (yes)	1.330	0.913-1.938	.137	.004	0.935	0.645-1.355	.721	.000			
Gender (female)	1.408	0.993-1.997	.055	.007	1.122	0.793-1.588	.515	.001			
Age (years)	0.999	0.983-1.015	.859	.000	1.002	0.986-1.018	.814	.000			
Ethnicity (Chinese)	1.000	-	-	.002	1.000	-	-	.018	1.000	-	-
(Malay)	0.942	0.650-1.366	.753		0.572	0.394-0.831	.003**		0.567	0.384-0.837	.004**
(Others)	0.686	0.381-1.237	.211		0.528	0.295-0.945	.032*		0.568	0.305-1.055	.073
Relationship status (without partner)	1.257	0.877-1.802	.213	.003	1.858	1.291-2.676	.001**	.021	1.827	1.245-2.682	.002**
Highest Qualification (Primary and below)	1.000	-	-	.000	1.000	-	-	.000			
(Secondary)	1.152	0.791-1.678	.462		0.890	0.612-1.293	.540				
(Tertiary)	1.082	0.644-1.817	.766		1.002	0.598-1.678	.993				
Employment (No formal employment) [a]	1.364	0.923-2.017	.120	.005	1.327	0.902-1.953	.151	.004			
Monthly Household Income [b] (<$2000)	1.106	0.747-1.639	.614	.002	1.308	0.883-1.937	.180	.004			
Living Arrangement (home owner)	0.869	0.610-1.236	.434	.002	1.198	0.843-1.702	.314	.000			
Housing (1-2 room public housing)	1.000	-	-	.020	1.000	-	-	.000			
(3-4 room public housing)	0.918	0.530-1.591	.761		1.128	0.651-1.954	.668				
(5 room public housing and above)	0.577	0.298-1.116	.102		0.820	0.427-1.573	.550				
Time on Dialysis (months)	0.998	0.995-1.002	.362	.002	1.000	0.997-1.004	.864	.000			
Charlson Comorbidity Index	1.028	0.970-1.089	.355	.002	0.985	0.930-1.044	.608	.001			

Potassium (mmol/l)	0.804	0.613-1.055	.115	.005	0.939	0.719-1.226	.643	.000			
Phosphate (mmol/l)	1.030	0.962-1.104	.396	.002	1.132	1.000-1.281	.050*	.012	1.129	0.991-1.286	.067
Haemoglobin (g/dl)	1.002	0.894-1.123	.976	.000	1.061	0.946-1.189	.313	.002			
Albumin (g/dl)	0.966	0.921-1.013	.156	.004	0.944	0.899-0.991	.021*	.011	0.932	0.887-0.980	.006**
Kt/V	1.172	0.766-1.793	.465	.001	1.043	0.689-1.579	.843	.000			

* $p < .05$, ** $p < .01$

OR: Odds ratios; CI: Confidence intervals

[a] Includes those who are retired, unemployed, or indicated 'Others'

[b] N=27 participants ticked option 'do not wish to answer' and N = 71 indicated 'don't know' and were excluded

R^2 for multivariate model = .061

Discussion

In general, our findings showed high prevalence for both anxiety and depression in ESRD patients, with figures consistent with reports from other countries [18,19], calling forth need for screening and interventions. A number of treatment approaches have been applied to patients with comorbid depression and long-term conditions, including pharmacotherapy, non-pharmacological approaches (e.g. cognitive behavioral therapy), and health systems interventions (e.g. collaborative care teams). More work is needed to explore how these can be applied in dialysis settings.

Contrary to our expectations, emotional adjustment outcomes were largely equivalent between DM ESRD and non-DM ESRD patients. Symptoms of depression were also levelled across groups. Only mean anxiety levels were significantly higher in DM ESRD, yet scores were still within normal range. Hence, the observed difference of 1 point in HADS-Anxiety while statistically significant is unlikely to be clinically significant. To this end, it is noteworthy that rates of anxiety and depression caseness, shown to prognosticate poor clinical outcomes [20] were comparable for DM ESRD and non-DM ESRD patients in both casemix-adjusted and unadjusted comparisons. This pattern of results is striking considering that DM ESRD patients have substantially greater comorbid burden, which previous work has shown to be related to distress indicators [21]. Nonetheless, the uniform psychological responses indicate that parameters other than comorbid burden/disease severity may be better suited to identify patients more at risk for distress. To this end, our findings underscore the importance of sociocultural factors.

Consistent with previous research, we found that single/unpartnered patients were shown to be at increased risk for depression relative to those married /partnered. The observed associations between depression caseness and relationship status are likely to reflect

the effects of low social support [22] in unpartnered individuals. Single/unpartnered status may also imply limited availability of emotional, substantive and instrumental resources (e.g. transportation, daily assistance).

The association with ethnicity is quite compelling, and differences in cultural beliefs and norms may explain the differential impact across ethnic groups. Chinese families tend to hold strongly to social-role obligations such that chronic conditions can be sources of frustration, tension and guilt. In Malay families on the other hand, the patient is more willingly released from such obligations [23]. Malay individuals may also possess strong protective factors such as increased religiosity [24] and strong informal social networks [25], whereas Chinese tend to rely more on self-directed coping strategies [26]. While more work and further replication is imperative, these findings suggest the need for providers to be vigilant for depression among patients with Chinese ancestry.

The only clinical parameter associated with depression was albumin – with lower albumin associated with higher odds of depression. This corroborates past findings that depressed patients tend to exhibit poorer nutritional status [27], and thereby poorer health outcomes [28]. Providers may consider screening for depression among patients with reduced albumin levels.

Interestingly, none of the parameters examined were associated with anxiety caseness; hence segmentation based on socio-demographic or clinical profile is not supported, contrary to previous work in non-Asian settings [29]. Factors such as illness beliefs have strong associations with depression [30] and may also be important in explaining symptoms of anxiety. Nevertheless, these findings underscore the importance of screening and monitoring symptoms for all renal care patients.

Study limitations need to be noted. First, the cross-sectional design does not allow us to determine causal relationships or course of distress over time. Longitudinal work is needed to map outcome trajectories across patient segments. Screening for eligibility was based on medical history with no formal cognitive diagnostic evaluation. Also, caseness was based on self-report data. While established cut-offs were used to allow comparability with previous work, these have yet to be validated for Mandarin and Malay versions. Diagnostic interviews have greater sensitivity and specificity and should be preferred for future work [4].

Conclusion

Rates of anxiety and depression are high within the ESRD population, and efforts should be made to monitor and alleviate such symptoms where they occur. Comorbid burden or diabetes was not associated with increased risk for anxiety and depression. Ethnicity, relationship status, and poor nutritional status were indicative of depression yet none of the parameters predicted anxiety caseness. The study highlights the importance of sociocultural factors in screening patients for depression, regardless of health status, so as to provide timely and appropriate care.

Declaration of Interests

The authors have no competing interests to report.

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