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# Appetite and Gastrointestinal Symptoms in End Stage Renal Disease Patients

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## Abstract

Poor appetite and gastrointestinal symptoms are common amongst dialysis patients. Often, this can lead to protein energy wasting, malnutrition and adverse outcomes. This study attempted to investigate the occurrence of these symptoms in haemodialysis (HD), peritoneal dialysis (PD), pre-dialysis chronic kidney disease (CKD5-ND) and control participants.

There were 306 participants in this study; 106 HD, 50 PD, 50 CKD5-ND and 100 control participants. Gastrointestinal symptoms were experienced by 81%, 72% and 51% of all End Stage Renal Disease (ESRD), CKD5-ND and control patients respectively ( $p < 0.05$ ). Poor appetite was reported by 10%, 26% and 1% of ESRD, CKD5-ND and control patients respectively ( $p < 0.05$ ). HD patients experienced more abdominal pain than PD patients and CKD5-ND patients were more likely to have dysgeusia. The occurrence of GI symptoms was not related to clinical variables (serum haemoglobin, albumin, urea and creatinine) but poor appetite was significantly associated to lower levels of serum urea and creatinine in dialysis patients ( $p < 0.05$ ). The presence of diabetes mellitus was associated with the development of GI symptoms, but not hypertension.

This study has raised awareness of the varied demographics of patients with poor appetite and gastrointestinal symptoms and measures have been implemented to improve appetite and gastrointestinal symptoms through focused and concerted efforts by doctors, nurses, nutritionists and dieticians. It is hoped that such measures might be beneficial in improving long term prognosis and quality of life of dialysis and CKD patients.

## Background

Patients with End Stage Renal Disease (ESRD) frequently complain of poor appetite and gastrointestinal symptoms. Patients with poor appetite have been linked with protein energy wasting (PEW) [1] and poor long term outcomes [2,3]. Poor long term outcomes could be related to cardiogenic

complications relating to non-atherosclerotic cardiovascular disease [4]. Likewise, patients with gastrointestinal symptoms can contribute to poor appetite [5], poorer quality of life [6], malnutrition [7] and psychosomatic diseases [7,8]. Many factors were implicated including underlying medical conditions (like Diabetes Mellitus), polypharmacy and psychosomatic symptoms. Few studies have reported on the differences between ESRD modalities (haemodialysis and peritoneal dialysis) with pre-dialysis (CKD5-ND) and control patients.

We hypothesized that there were differences in how dialysis, CKD5-ND and control patients perceived their appetites and gastrointestinal symptoms. This cross-sectional questionnaire study was carried out to investigate these differences, with emphasis on correlations with demographic factors (gender, age and race), co-existing medical conditions (diabetes mellitus or hypertension), dialysis adequacy, serum haematological and biochemical parameters (haemoglobin, albumin, urea and creatinine). We hoped to use information from this study to promote dietary and nutritional changes to a targeted group of CKD patients in the hope of improving quality of life and long term survival outcomes.

## Methods

Inclusion criteria for the study include patients with ESRD who were undergoing HD or PD from the National Dialysis Centre. Additionally, CKD5-ND patients were recruited from our CKD clinics of the tertiary teaching hospital were invited to participate in the study. Exclusion criteria include patients less than 18 years of age, with a strong history of non-compliance with medication and treatment, with recent hospitalization (within 3 months) and have evidence of recent active infections (including bacterial and viral). Age and gender matched controls were family members or carers that accompanied the patients to dialysis centres and outpatient clinics. The study was conducted through a face-to-face interview to ensure that patients understood the questions and that immediate help could be obtained for them if the symptoms were deemed severe enough.

Apart from demographic data, specific questions were asked about appetite (quality, changes) and gastrointestinal symptoms

(taste, hiccups, satiety, nausea, vomiting, indigestion, abdominal pain, bloating, constipation and diarrhoea) in the last three months. Details on blood parameters, co-morbid conditions, medications and duration of dialysis were retrieved from medical notes. Most of the questions in the questionnaire required a 'yes' or 'no' response. Poor appetite is defined as decreased desire to eat any meals. For GI symptoms where there are several terminologies (dyspepsia, indigestion and heartburn), only the most commonly used terminology was used. For some of these symptoms, enquiries were supplemented with symptom descriptions (i.e. pain or discomfort located in the epigastric area for dyspepsia and in the retro-sternum area for heartburn) to confirm the presence of symptoms. For other GI symptoms, the terminologies were quite specific. Definitions of GI symptoms follow standard accepted definitions. Dyspepsia was defined as burning pain or discomfort that was centered in the epigastrium. Heartburn was defined as the presence of a retrosternal burning pain or discomfort with or without associated regurgitation. Nausea was defined as the sensation of wanting to vomit but without vomiting. Dysphagia and odynophagia were defined as difficulty in swallowing or feeling of food getting stuck after swallowing and painful swallowing respectively. Non-epigastric pain was defined as any other pain that is not centered in the epigastric region. Diarrhoea and constipation were defined as stool frequency of more than three times per day and less than three times per week respectively. Parts of this questionnaire have been used and validated in a similar study investigating the association between psychosomatic and lower gastrointestinal symptoms in dialysis patients [9].

Data were coded and entered into the Statistical Package for Social Sciences program (SPSS) for analysis. Comparisons were made between patients from different modalities of RRT and controls for the presence of gastrointestinal symptoms and quality of appetite. Among patients with ESRD, correlations were made between co-existing medical conditions and dialysis parameters with the presence of GI symptoms and quality of appetite. Continuous variables were compared using either Student's t-test or Mann-Whitney test, whereas the categorical variables were compared with  $\chi^2$  and Fisher's exact test where appropriate. Level of significance was taken as  $p < 0.05$ .

## Results

A total of 306 respondents participated in the study. There were 106 HD, 50 PD, 50 CKD5-ND and 100 control participants. Hypertension (39%) and diabetes mellitus (35%) were the two primary causes of ESRD. The mean urea reduction ratio (HD patients), kt/V (PD patients) and body mass index were 0.7, 1.9 and 25.2, respectively. Routine blood tests showed mean serum haemoglobin, albumin, creatinine and urea of 9.6 g/dL, 35.3 g/dL, 818.3  $\mu\text{mol/dL}$  and 18.0 mmol/L, respectively. There was a female preponderance (56% vs 44%). Other demographic data for ESRD patients were illustrated in Table 1.

**Table 1:** Demographic and Clinical Factors of participants (HD, PD, CKD 5-ND and control that participate in the study); BMI= Body Mass Index; SD= Standard Deviation; IQR= Interquartile Range; HD= Haemodialysis; PD= Peritoneal Dialysis; a) The

distribution is skewed to the right; b) Many patients have co-existing conditions especially hypertension and diabetes; URR= Urea Reduction Ratio; measures adequacy of renal replacement therapy for HD patients;  $>65.0\%$  indicate a good dialysis;  $<65.0\%$  indicates poor dialysis. Kt/V= Dialysis Efficacy; measures adequacy of renal replacement therapy for PD patients;  $>1.8$  indicate a good dialysis;  $<1.8$  indicate poor dialysis.

Variable	Mean (SD)	Median (IQR)	n (%)
Age (years)	53.8 (16.3)	-	-
Gender			
Male	-	-	134 (43.8%)
Female	-	-	172 (56.2%)
Race			
Malay	-	-	268 (87.6%)
Non-malay	-	-	38 (12.4%)
Primary cause of ESRD			
Hypertension	-	-	102 (39.2%) <sup>b</sup>
Diabetes	-	-	108 (35.3%) <sup>b</sup>
Others	-	-	79 (25.8%) <sup>b</sup>
URR (HD)	-	0.7 (0.14) <sup>a</sup>	-
Kt/V (PD)	-	1.9 (0.78)	-
BMI (kg/m <sup>2</sup> )	-	25.2 (6.59) <sup>a</sup>	-
Hemoglobin (g/dL)	9.6 (4.30)	-	-
Serum albumin (g/dL)	35.3 (11.00)	-	-
Creatinine ( $\mu\text{mol/dL}$ )	818.3 (380.81)	-	-
Serum urea (mmol/L)	18.0 (8.91) <sup>a</sup>	-	-

81% of all ESRD patients experienced GI symptoms, with early satiety (48%), indigestion (40%), nausea (30%) and constipation (30%) as the most commonly reported symptoms (Table 2). Compared to controls, ESRD and CKD5-ND patients were more likely to suffer from early satiety, nausea, vomiting, indigestion, constipation, change in taste (dysgeusia) and poor appetite (all  $p < 0.05$ ). Additionally, CKD5-ND patients had worse appetite and dysgeusia than ESRD patients (Table 2). HD and PD patients had similar incidence of GI symptoms and poor appetite, but the former group were more likely to experience abdominal pain (Table 3). The occurrence of GI symptoms was not related to clinical variables (serum haemoglobin, albumin, urea and creatinine) but poor appetite was significantly associated to lower levels of serum urea and creatinine (Table 4). There was also a non-statistically significant relationship between poor appetite with serum haemoglobin ( $p = 0.164$ ) and serum albumin

( $p=0.142$ ). Diabetes mellitus was associated with more GI symptoms but not with poor appetite.

**Table 2:** Comparison of GI symptoms and appetite in dialysis patients, CDK5-ND and control patients; a) Chi-square test for independence; GI= Gastrointestinal symptoms; \*Poor Appetite: Very good, good and fair appetite = NO, poor and very poor appetite = YES; CDK5-ND= chronic kidney disease stage 5 - non-dialysis.

Variable	GI symptoms	Dialysis patients	CDK 5-ND patients	Controls	$\chi^2$ statistic a (df)	P value
		(n=156) n (%)	(n=50) n (%)	(n=100) n (%)		
Any GI symptoms	Yes	126 (80.8%)	36 (72.0%)	51 (51.0%)	25.69 (2)	< 0.001
	No	30 (19.2%)	14 (28.0%)	49 (49.0%)		
Hiccups	Yes	40 (25.6%)	11 (22.0%)	27 (27.0%)	0.44 (2)	0.801
	No	116 (74.4%)	39 (78.0%)	73 (73.0%)		
Early satiety	Yes	75 (48.1%)	23 (46.0%)	13 (13.0%)	34.88 (2)	<0.001
	No	81 (51.9%)	27 (54.0%)	87 (87.0%)		
Nausea	Yes	47 (30.1%)	18 (36.0%)	11 (11.0%)	15.93 (2)	<0.001
	No	109 (69.9%)	32 (64.0%)	89 (89.0%)		
Vomiting	Yes	39 (25.0%)	10 (20.0%)	11 (11.0%)	7.58 (2)	0.023
	No	117 (75.0%)	40 (80.0%)	89 (89.0%)		
Indigestion	Yes	62 (39.7%)	21 (42.0%)	18 (18.0%)	15.21 (2)	<0.001
	No	94 (60.3%)	29 (58.0%)	82 (82.0%)		
Abdominal pain	Yes	26 (16.7%)	6 (12.0%)	13 (13.0%)	1.00 (2)	0.606
	No	130 (83.3%)	44 (88.0%)	87 (87.0%)		
Bloating	Yes	32 (20.5%)	8 (16.0%)	10 (10.0%)	4.93 (2)	0.085

Symptom	Response	Dialysis			$\chi^2$ statistic (df)	P value
		n (%)	n (%)	n (%)		
Constipation	No	124 (79.5%)	42 (84.0%)	90 (90.0%)	10.08 (2)	0.006
	Yes	47 (30.1%)	11 (22.0%)	13 (13.0%)		
Diarrhoea	No	109 (69.9%)	39 (78.0%)	87 (87.0%)	1.91 (2)	0.385
	Yes	13 (8.3%)	4 (8.0%)	4 (4.0%)		
Change of taste	No	122 (78.2%)	29 (58.0%)	98 (98.0%)	37.29 (2)	<0.001
	Yes	34 (21.8%)	21 (42.0%)	2 (2.0%)		
Poor Appetite	No	141 (90.4%)	37 (74.0%)	99 (99.0%)	24.29 (2)	<0.001
	Yes	15 (9.6%)	13 (26.0%)	1 (1.0%)		

**Table 3:** Comparison of prevalence of GI symptoms between HD and PD

Patients Variable	GI symptoms	Dialysis		$\chi^2$ statistic (df)	P value
		HD (n=101) n (%)	PD (n=55) n (%)		
Any GI symptoms	Yes	84 (83.2%)	42 (76.4%)	1.06 (1)	0.303
	No	17 (16.8%)	13 (23.6%)		
Hiccups	Yes	29 (28.7%)	11 (20.0%)	1.41 (1)	0.234
	No	72 (71.3%)	44 (80.0%)		
Early satiety	Yes	52 (51.5%)	23 (41.8%)	1.33 (1)	0.248
	No	49 (48.5%)	32 (58.2%)		
Nausea	Yes	32 (31.7%)	15 (27.3%)	0.329 (1)	0.556
	No	69 (68.3%)	40 (72.7%)		

Vomiting	Yes	25 (24.8%)	14 (25.5%)	0.009 (1)	0.92 3
	No	76 (75.2%)	41 (74.5%)		
Indigestion	Yes	44 (43.6%)	18 (32.7%)	1.75 (1)	0.18 6
	No	57 (56.4%)	37 (67.3%)		
Abdominal pain	Yes	22 (21.8%)	4 (7.3%)	5.40 (1)	0.02
	No	79 (78.2%)	51 (92.7%)		
Bloating	Yes	24 (23.8%)	8 (14.5%)	1.86 (1)	0.17 3
	No	77 (76.2%)	47 (85.5%)		
Constipation	Yes	32 (31.7%)	15 (27.3%)	0.329 (1)	0.56 6
	No	69 (68.3%)	40 (72.7%)		
Diarrhoea	Yes	8 (7.9%)	5 (90.1%)	0.064 (1)	0.80 1
	No	93 (92.1%)	50 (90.9%)		
Poor Appetite	Yes	11 (10.9%)	4(7.3%)	0.536 (1)	0.46 4
	No	90 (89.1%)	51 (92.7%)		
Change of taste	Yes	21 (20.8%)	13 (23.6%)	0.169 (1)	0.68 1
	No	80 (79.2%)	42 (76.3%)		

**Table 4:** Association between clinical factors in dialysis patients;  
<sup>a</sup>Independent t test

		Serum haemoglobin (g/dL)	Serum Albumin (g/dL)	Serum Urea (mmol/L)	Serum Creatinine (Umol/L)
GI Symptoms	Yes (n=126)	10.4 (2.00)	37.6 (5.90)	17.5 (5.91)	905.4 (345.84)
	No (n=30)	10.8 (1.69)	37.8 (3.60)	17.3 (4.33)	950.3 (240.04)

		-0.3 (-1.0, 0.5)	-0.2 (-1.85, 2.05)	0.2 (-2.1, 2.5)	-45 (-176.8, 86.9)
	t statistic (df) <sup>a</sup>	-0.8 (154)	-1.51(154)	-1.51 (154)	-0.67 (154)
	P value <sup>a</sup>	0.425	0.88	0.879	0.502
Poor appetite	Yes (n=15)	9.8 (1.37)	35.7 (4.79)	14.0 (4.95)	646.4 (209.48)
	No (n=141)	10.6 (1.98)	37.9 (5.57)	17.9 (5.62)	942.5 (325.88)
	(95 % CI)	-0.7 (-1.8,0.3)	-2.2 (-5.2,0.7)	-3.9 (-6.8, -0.9)	-296.1 (-466.2, -126.0)
	t statistic (df) <sup>a</sup>	-1.40 (154)	-1.48 (154)	-2.56 (154)	-3.44 (154)
	P value <sup>a</sup>	0.164	0.142	0.011	0.001

## Discussion

This study showed that ESRD and CKD5-ND patients were more likely to experience poor appetite and GI symptoms than controls. These findings were not unusual and have been reported in numerous case series. The uniqueness of this study lied with the fact that we were able to compare prevalence of symptoms in ESRD patients with pre-dialysis (CKD5- ND) patients and controls. Whilst the literature was almost unanimous in reporting a higher prevalence of GI symptoms in ESRD patients, there were inconsistencies in reporting prevalence between HD and PD patients. Our literature review from pub med revealed 8 studies investigating the differences between these two groups of patients (Table 5). The general feeling was that PD patients were more likely to get reflux symptoms [10-14]. HD patients, on the other hand had more constipation [10,14] and abdominal pain [8,15]. This study confirmed the association of abdominal pain with HD, but not other symptoms. Our local experience indicated that this could be related to non-occlusive mesenteric ischaemia (NOMI) which has been seen in numerous patients under our care. We suspected that this often under-reported phenomenon was particularly prevalent in our HD population due to numerous factors like intra-dialytic hypotension (leading to splanchnic hypoperfusion) and inherent atherosclerotic risks of patients. The interviews were also carried out during or after the time patients had dialysis and this might have inadvertently increased the likelihood of abdominal pain reporting.

**Table 5:** Literature review of studies comparing GI symptoms in HD and PD patients.

Author/Year/Country/Reference	Patients	Results
Farhana et al. / 2014 / Brunei	100 HD patients,	Constipation is more common among HD patients.
	50 PD patients,	
	50 CKD5-ND patients,	
	100 controls	

Yasuda et al. / 2002 / Japan [10]	268 HD patients,	Constipation occurs less frequently in CAPD patients
	204 CAPD patients,	
	No control	
Strid et al. / 2002 / Sweden [7]	128 HD patients,	PD patients have more severe reflux and eating dysfunction.
	55 PD patients,	
	50 Pre-dialysis	
	2162 controls	
Kahvecioglu et al. / 2005 / Turkey [8]	93 Hd patients,	Epigastric pain is more prevalent in HD patients
	35 PD patients,	
	51 controls	
Cano et al. / 2007 / UK [11]	100 Hd patients	No significant difference between PD and HD
	48 PD patients,	
	148 controls	
Strid et al. (2009) / Sweden [12]	157 HD patients	Dyspepsia is more common in PD patients
	112 PD patients	
Anderson JE / 1999 / Adv Perit Dial [13]		GERD is more common in PD patients
Dong et al. / 2014 / China / World Journal of gastroenterology [14]	182 HD patients	PD patients have higher reflux and eating dysfunction.
	112 Pd patients	HD patients have more diarrhea, constipation and abdominal pain
Salamon K / J Ren Nutr / 2013 [15]	172 HD patients	PD patients report more GI side effects and decrease in food intake
	122 Pd patients	

Interestingly, there was no major difference in perception of GI symptoms between ESRD and CKD5-ND patients. Quite understandably, pre-dialysis patients experienced a greater change in taste (dysgeusia) possibly related to oral and salivary changes caused by high concentration of urea in the saliva which is broken down to ammonia by urease [16,17]. Presumably, dialysis will partially correct the uremia leading to tolerable dysgeusic symptoms in the prevailing dialysis population. CKD5-ND patients also suffered from poorer appetite compared to ESRD patients, likely from uncorrected uremia and poorer psychosocial mental state (usually arising from anxiety from having to start dialysis soon). Like the dialysis population, CKD5-ND patients experienced more overall GI symptoms and had poorer appetite than controls. This was consistent with other studies which investigated GI symptoms in CKD patients [7,18].

The prevalence of GI symptoms in ESRD patients is well described. The aetiology is likely to be multifactorial ranging from effect of ESRD and treatment on the GI tract, diet, medications and other co-morbid conditions. A similar study was conducted in 2010 which compared GI and psychosomatic symptoms between HD patients and controls in the same population [9]. This study confirmed that GI symptoms were common among Asian patients but did not make comparisons with appetite nor with PD patients and CKD5-ND patients. The

motivation to emulate and improve on the previous study was to provide evidence for a more targeted approach on improving nutrition and well-being in the sub-set of dialysis population that were anorexic and malnourished. Protein energy wasting (PEW) has previously been demonstrated in a similar dialysis population in Malaysia where poor appetite was associated with patients with lower lean tissue and fat mass, lower levels of serum urea and creatinine, higher dialysis malnutrition score and poorer physical and mental health scores [19]. Protein energy wasting has been widely accepted as a major factor in determining prognosis of dialysis patients [20]. The evidence for increased mortality was similar in both PD [21] and HD [22] patients. The study also revealed that poor appetite was not limited to dialysis patients as CKD5-ND patients also displayed similar anorexic symptoms, consistent with other studies published [23]. Another study reported that poor appetite affected survival in PD patients but not CKD5-ND patients [24]. The results of this study have heightened our awareness of poor appetite in our patients, particularly those with lower levels of serum urea, creatinine and albumin. This has enabled us to help through a more targeted and concerted approach by selectively counselling and providing intensive nutritional support for patients in need of such interventions. We are now more likely to refer patients to gastroenterology to evaluate and alleviate resistant GI symptoms and to investigate potentially reversible GI tract triggers.

This study is limited by the small number of PD (n=50) and CKD5-ND (n=50) participants. The country only has about 60-70 PD patients [25] and the majority has been recruited for this study. We also felt that some of the CKD5-ND patients were afraid to disclose any symptoms to our doctors because they fear that it may lead to them being started prematurely on dialysis. On the other hand, there may be some recruitment bias in the participation selection process. Patients who have GI symptoms or poor appetite were more likely to volunteer to participate as they might have hoped that the researchers might be able to intervene and alleviate their problems. We also felt that the face-to-face nature of the interview make patients more likely to disclose and confide latent GI symptoms that would not have been revealed otherwise.

## Conclusion

Our study confirmed that our ESRD and CKD5-ND patients had high prevalence of GI symptoms and poor appetite. CKD5-ND patients also had symptoms associated with poor or change in taste. Abdominal pain was more common in HD patients and poor appetite was associated with lower levels of serum urea and creatinine. A more concerted and focused approach towards dealing with anorexia and malnourishment in dialysis patients has been advocated in light of the findings of this study and we hope that this will result in improvement in quality of life and long term prognosis.

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