

Prevalence and Associated Clinical Factors of Gastroesophageal Reflux Disease in Filipino Hemodialysis Patients: A Cross Sectional Study

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Abstract

Introduction: Reflux is one of the most common gastrointestinal symptoms among dialysis patients. This may be associated with several clinical factors such as comorbidities and subsequent polypharmacy. However, this remains unrecognized and untreated.

Objectives: The objectives of this study were to determine the prevalence of Gastroesophageal Reflux Disease (GERD) in Filipino patients on maintenance hemodialysis (HD) and to investigate associated demographic, clinical, and renal profiles of HD patients with and without GERD.

Methods: This was a cross-sectional, multicenter study using a validated GERD questionnaire (GERDQ) translated into Filipino. Patients above 18 years old undergoing hemodialysis as outpatients were included. Several clinical factors such as demographic, clinical, and renal profiles were analyzed based on the absence and presence of GERD with a predetermined cut-off value of eight or above.

Results: Included in our analysis were 264 patients, from which 36 had GERDQ score of ≥ 8 (13.64% 95%CI 9.98-18.35). Factors associated with having score of ≥ 8 included the following: (1) having chronic heart disease or CHD (COR 4.041, 95%CI 1.89-8.64, $p<0.001$), (2) being on insulin (COR 2.599, 95%CI 1.25-5.42, $p=0.011$), (3) anemia (COR 4.508, 95%CI 1.91-10.64, $p=0.001$) (4) diagnosis of both hypertensive kidney disease and diabetes kidney disease (COR 3.853, 95%CI 1.15-12.96, $p=0.029$), (5) previous diagnosis of GERD (COR 6.655, 95%CI 3.18-13.91, $p<0.001$), (6) previous intake of antacids (COR 2.622, 95%CI 1.17-5.89, $p=0.020$), (7) being employed (COR 2.332, 95%CI 1.15-4.75, $p=0.020$) (8) alcohol consumption (COR 2.477, 95%CI 1.23-5.01, $p=0.012$), and (9) smoking (COR 2.405, 95%CI 1.19-4.86, $p=0.014$).

Conclusion: In our study, the prevalence of GERD in Filipino HD patients was 13.64% and may be associated with several clinical factors such as heart disease, insulin use, anemia, hypertension, diabetic kidney disease, previous diagnosis of GERD, use of antacids, being employed, smoking, and alcohol use. A comprehensive understanding of the relationships between these clinical factors awaits further studies in a larger number of patients.

Keywords: GERD, GERDQ, Filipino translation, Chronic Kidney Disease, Hemodialysis

Introduction

GERD is defined as the condition which develops when the reflux of stomach contents causes troublesome symptoms and complications with a pooled prevalence of 14% in the general population. Among Southeast Asian nations, a lower rate is reported at 7.4%.¹⁻³ Chronic kidney disease (CKD) patients commonly experience gastrointestinal symptoms, but there seems to be a

disconnect between patient perceptions and clinical definitions of normal or abnormal gastrointestinal health.⁴ The prevalence of GI symptoms, including gastroesophageal reflux, causes significant impairment in activities of daily life and, when present in patients can further lower the quality of life.⁵⁻⁷ One of the most common GI symptoms in dialysis patients is reflux, but the association between GERD and end-stage renal disease (ESRD) remains unclear.^{8,9} Kawaguchi et al. concluded that the prevalence of GERD is increased in chronic renal failure patients, which was especially noted in HD patients although the risk factors were not clear.¹⁰ It has been reported that in HD patients suffering from GERD, there is a positive correlation with the duration of

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dialysis, severity of renal failure, diabetes mellitus, smoking, and body mass index and a negative correlation between dialysis modalities, age, gender, use of NSAID and hypoalbuminemia, although these needs further evaluation.¹¹

Furthermore, CKD coexists with many other comorbidities, particularly heart disease, and therefore requires polypharmacy in many instances. In these patients, identifying and controlling symptoms of GERD is important not only to ensure adherence to their oral maintenance medications but to differentiate it as well from atypical angina that is frequent in this patient population without the need for specialist referral.¹² Fortunately, upper endoscopy is generally not required for the diagnosis of GERD, especially when symptoms are typical and respond to therapy.¹³ Latest guidelines then suggest the use of a locally validated standardized questionnaire (GERDQ) to reinforce clinical diagnosis of GERD in which a linguistic validation study with regional Filipino translation is made available by Castillo-Carandang et al.^{14,15}

GERDQ is a well-developed questionnaire derived from the DIAMOND study, which includes primary care patients with upper GI symptoms. Clinical diagnosis and questionnaire scores were compared with objective diagnostic tests for GERD such as endoscopy and 24-hour pH-monitoring, Symptom Association Probability, and Proton pump inhibitor test to develop a questionnaire with high diagnostic accuracy for GERD.¹⁶ Questions were derived from other validated questionnaires and has a symptom-based sensitivity and specificity of 65% and 71%, respectively. The performance of the GERDQ is similar with the diagnosis of GERD when made by a gastroenterologist at a sensitivity and specificity of 67% and 70%, respectively.¹⁷ A pooled analysis of cluster-randomized studies concluded that the primary management of GERD can actually be improved using GERDQ rather than standard treatment.¹⁸ In addition, this symptom-based approach is non-inferior to those diagnosed with endoscopy.¹⁹

Objectives. The objectives of this study were to determine the prevalence of GERD in Filipino patients on maintenance HD using the validated GERDQ questionnaire and to investigate associated demographic, clinical, and renal profiles of HD patients with and without GERD.

Methods

This was a cross-sectional, multicenter study with the participants coming from outpatient hemodialysis units of the following tertiary hospitals: Central Luzon Doctors' Hospital, Jecsons' Medical Center, and Ramos General Hospital in Tarlac City, Philippines. The survey was conducted from June to October 2021. Included were ESRD patients > 18 years old and undergoing regular HD. Excluded were those unable to answer the questionnaire, patients with cognitive impairment, patients who did not provide consent, critically-ill, and those who underwent abdominal surgical procedures in the last three months.

After obtaining informed written consent, patients were interviewed by independent dedicated personnel and asked about their symptoms using GERDQ (Appendix A) which is utilized to reinforce the diagnosis of GERD. GERDQ scores the frequency of four symptom questions: 1) Heartburn, 2) Regurgitation, 3) Dyspepsia and 4) Nausea and two impact questions: 1) Sleep disturbance and 2) Need for over-the-counter medications during the past seven days. It uses a 4-point scale with scores ranging from 0 to 3 (0 = 0 days/week; 1 = 1 day/week; 2 = 2-3 days/ week; and 3 = 4-7 days/week). A predetermined cut-off GERDQ score of 8 or more was regarded as having GERD.

Patient clinical profiles were also obtained. Information regarding previous diagnosis of GERD and previous intake of antacids such as proton pump inhibitors, H₂-receptor antagonists, aluminum/magnesium tablets, or alginates were obtained. Presence of comorbidities such as diabetes mellitus, hypertension, chronic heart and lung diseases, cerebrovascular diseases, hematologic disorders, malignancies, and immunocompromised states, along with their maintenance medications, including antihypertensives (ACE Inhibitors, angiotensin receptor blockers, beta-blockers, calcium channel blockers, diuretics, vasodilators), anti-diabetic medications (insulin and oral hypoglycemic agents), antiplatelets and anticoagulants and maintenance medications for CKD (iron supplements, sodium bicarbonate, calcium carbonate, erythropoietin stimulating agents and potassium binders) were also collected.

Table I. Demographic Profile of Patients (%)

Parameter	Total (n=264)	GERD (n=36)	Without GERD (n=228)	p-value
Sex				0.805*
Male	149 (56.44)	21 (58.33)	128 (56.14)	
Female	115 (43.56)	15 (41.67)	100 (43.86)	
Age, years (Median, Range)	55.5 (22–90)	56.5 (32–73)	55 (22–90)	0.921†
Civil status				0.145*
Single	33 (12.5)	3 (8.33)	30 (13.16)	
Married	196 (74.24)	24 (66.67)	172 (75.44)	
Divorced	5 (1.89)	1 (2.78)	4 (1.75)	
Widowed	30 (11.36)	8 (22.22)	22 (9.65)	
Employment Status				0.019*
Without	151 (57.2)	14 (38.89)	137 (60.09)	
With	113 (42.8)	22 (61.11)	91 (39.91)	

Statistical tests used: * Fisher's Exact/Chi-square test; † Mann-Whitney U-test

Table II. Clinical Profile of Patients (%)

Parameter	Total (n=264)	GERD (n=36)	Without GERD (n=228)	p-value
Comorbidities				
Hypertension	198 (75)	25 (69.44)	173 (75.88)	0.412*
Diabetes Mellitus	133 (50.38)	23 (63.89)	110 (48.25)	0.106*
Chronic heart disease	45 (17.05)	14 (38.89)	31 (13.6)	0.001*
Cerebrovascular disease	34 (12.88)	5 (13.89)	29 (12.72)	0.792*
Anemia	28 (10.61)	10 (27.78)	18 (7.89)	0.001*
Chronic lung disease	9 (3.41)	2 (5.56)	7 (3.07)	0.353*
Cancer	2 (0.76)	1 (2.78)	1 (0.44)	0.255*
Gout	11 (4.17)	2 (5.56)	9 (3.95)	0.650*
Other	25 (9.47)	6 (16.67)	19 (8.33)	0.126*
Previously diagnosed with GERD	60 (22.73)	21 (58.33)	39 (17.11)	<0.001*
Previously took antacid ^a	156 (59.09)	28 (77.78)	128 (56.14)	0.017*
Maintenance Medications				
ACE Inhibitor	1 (0.38)	0	1 (0.44)	>0.999*
Angiotensin Receptor Blocker	115 (43.56)	17 (47.22)	98 (42.98)	0.718*
Alpha Adrenergic Agonist	87 (32.95)	13 (36.11)	74 (32.46)	0.704*
Beta-Blocker	59 (22.35)	8 (22.22)	51 (22.37)	>0.999*
Calcium Channel Blocker	139 (52.65)	19 (52.78)	120 (52.63)	>0.999*
Diuretics	26 (9.85)	5 (13.89)	21 (9.21)	0.370*
Iron Supplement	241 (91.29)	28 (77.78)	213 (93.42)	0.006*
Sodium Bicarbonate	196 (74.24)	24 (66.67)	172 (75.44)	0.305*
Calcium Carbonate	188 (71.21)	26 (72.22)	162 (71.05)	>0.999*
Erythropoietin Injection	244 (92.42)	32 (88.89)	212 (92.98)	0.493*
Antiplatelet	51 (19.32)	8 (22.22)	43 (18.86)	0.651*
Anticoagulant	6 (2.27)	2 (5.56)	4 (1.75)	0.191*
Insulin	59 (22.35)	14 (38.89)	45 (19.74)	0.017*
Oral Antidiabetic	55 (20.83)	8 (22.22)	47 (20.61)	0.827*
Nitrates	6 (2.27)	2 (5.56)	4 (1.75)	0.191*
Statin	89 (33.71)	15 (41.67)	74 (32.46)	0.343*
Related history				>0.999*
Alcohol consumption	7 (7.14)	1 (5)	6 (7.69)	
Smoking	2 (2.04)	0	2 (2.56)	
Both alcohol and smoking	89 (90.82)	19 (95)	70 (89.74)	
Diagnosis				0.160*
Congenital kidney Disease	2 (0.76)	0	2 (0.88)	
Diabetic Kidney Disease	62 (23.48)	9 (25)	53 (23.25)	
Glomerulonephritis	21 (7.95)	1 (2.78)	20 (8.77)	
Gouty nephropathy	13 (4.92)	3 (8.33)	10 (4.39)	
Hepatorenal syndrome	1 (0.38)	0	1 (0.44)	
Hypertensive Kidney Disease	125 (47.35)	14 (38.89)	111 (48.68)	
Hypertensive & Diabetic Kidney Disease	15 (5.68)	6 (16.67)	9 (3.95)	
Leptospirosis	2 (0.76)	0	2 (0.88)	
NSAID induced Nephropathy	13 (4.92)	3 (8.33)	10 (4.39)	
Polycystic Kidney Disease	8 (3.03)	0	8 (3.51)	
Post-obstructive Uropathy	2 (0.76)	0	2 (0.88)	
Years in dialysis	2 (0.1–10)	3 (0.3–10)	2 (0.1–9)	0.537†
Type of vascular access				0.783*
AV fistula	232 (87.88)	31 (86.11)	201 (88.16)	
Intra jugular	32 (12.12)	5 (13.89)	27 (11.84)	
Anticoagulation - Heparin	261 (98.86)	36 (100)	225 (98.68)	>0.999*
Frequency per week				0.053*
1	4 (1.52)	0	4 (1.75)	
2	211 (79.92)	24 (66.67)	187 (82.02)	
3	49 (18.56)	12 (33.33)	37 (16.23)	
Duration, hours	4 (2–5)	4 (2.5–4)	4 (2–5)	0.765†
Blood flow rate, ml/min	250 (150–365)	200 (150–300)	250 (150–365)	0.541†
Dialysate Flow Rate, ml/min	500 (300–650)	400 (300–600)	500 (300–650)	0.539†
Dialysis Modality				0.136*
Conventional	263 (99.62)	35 (97.22)	228 (100)	
Sequential	1 (0.38)	1 (2.78)	0	

^a Such as but not limited to H₂-receptor antagonist, Proton pump inhibitors, Aluminum/magnesium tablets, or Alginates

Statistical tests used: * Fisher's Exact/Chi-square test; † Mann-Whitney U-test

Dialysis profile which includes diagnoses, modality, duration, frequency, type of vascular access, blood and dialysate flow rate and the years in hemodialysis were identified and other relevant histories such as employment status, smoking, and alcohol consumption.

Description of Outcome Measures. The primary outcome of the study was the prevalence rate of GERD among HD patients using GERDQ. Secondary outcomes included associated factors such as patient demographic details (sex, age, civil status and employment), clinical (comorbidities and maintenance medications, previous diagnosis of GERD and previous use of antacids, smoking and alcohol use) and renal profiles (diagnosis and years on dialysis and hemodialysis parameters).

Sample Size Estimation. The sample size was calculated using the prevalence rate of GERD (13.98%) reported in a recent metanalysis in 2020.² We used a confidence interval of 95% and a margin of error of 0.05. The computed sample size was 185. We achieved an actual sample of 264 in this study implemented during the COVID-19 pandemic. All valid data were included in the analysis. Missing variables were neither replaced nor estimated.

Statistical Analysis. Descriptive statistics were used to summarize the general and clinical characteristics of the participants. Frequency and proportion were used for categorical variables (nominal/ordinal). *Shapiro-Wilk's* test was used to check for normality of interval/ratio variables such as age, years in dialysis, duration, blood flow rate, and dialysate flow rate. All interval/ratio variables were non-normally distributed, so median and range were used to describe

them. *Mann-Whitney U* test and *Fisher's Exact/Chi-square* test were used to compare the difference of median and frequency between those with GERD vs. those without GERD, respectively. Odds ratios (OR) and the corresponding 95% CI from *Firth's logistic regression*

Table III. GERDQ Responses of Patients (%)

	0 days	1 day	2-3 days	4-7 days
During the past week, how many days did you have a burning feeling behind your breastbone? (heartburn)	207 (78.41)	12 (4.55)	34 (12.88)	11 (4.17)
During the past week, how many days did you have stomach contents (liquid or solid) moving upwards toward your tongue or mouth? (regurgitation)	215 (81.44)	9 (3.41)	30 (11.36)	10 (3.79)
During the past week, how many days did you have a pain in the center of the stomach?	207 (78.41)	25 (9.47)	25 (9.47)	7 (2.65)
During the past week, how many days did you have nausea?	226 (85.61)	27 (10.23)	9 (3.41)	2 (0.76)
During the past week, how many days did you have difficulty getting a good night's sleep because of your heartburn or regurgitation?	238 (90.15)	18 (6.82)	8 (3.03)	0
During the past week, how many days did you take additional medication for your heartburn and/or regurgitation other than what the physician told you to take?	237 (89.77)	5 (1.89)	10 (3.79)	12 (4.55)

were computed to determine the association between patient profiles with GERD. All valid data were included in the analysis. Missing values were neither replaced nor estimated. Null hypothesis was rejected at $p < 0.05$ level of significance. STATA 15.0® was used for data analysis.

Ethical Considerations. The study protocol was approved by the University of the East Ramon Magsaysay Memorial Medical Center, Inc. Research Institute for Health Sciences Ethics Review Committee (RIHS ERC Code: 0893/E/2020/121). This study was conducted in accordance with the ethical guidelines in the Declaration of Helsinki.

Results

Included in our analysis are 264 patients, from which 36 had a GERDQ score of eight or higher (13.64%, 95% CI 9.98-18.35). Overall, 56% were male, the median age was 55.5 years (youngest was 22 and oldest was 90 years old), and 74% are married (Table I). We found that those with GERD were employed compared with those without GERD (61.11% vs. 39.91%, $p = 0.019$).

The clinical profile of the patients is listed in Table II. Between those with and without GERD, patients with GERD have higher frequencies of chronic heart disease (38.89% vs 13.6%, $p=0.001$) and anemia (27.78% vs 7.89%, $p=0.001$) as comorbidities; being previously diagnosed with GERD or reflux (58.33% vs 17.11%, $p<0.001$), previously taking antacid (77.78% vs 56.14%, $p=0.017$), and being on insulin (38.89% vs 19.74%, $p=0.017$). There were no notable differences in terms of cases of diabetes between the two groups, while the group without GERD had more patients taking iron supplements (93.42% vs. 77.78%, $p = 0.006$).

Based on GERDQ responses of the patients (Table III), the majority reported no symptoms of heartburn (78.41%), regurgitation (81.44%), epigastric pain (78.41%), nausea (85.61%), difficulty getting a good night's sleep (90.15%), and taking of additional medication (89.77%). For those who did report these symptoms, at most, 13% felt heartburn and 11% experienced regurgitation for 2 to 3 days, while 10% had nausea for one day.

Factors associated with having a GERDQ score of 8 and above includes the following: (1) having CHD (COR 4.041, 95% CI 1.89-8.64, $p<0.001$), (2) being on insulin (COR 2.599, 95%CI 1.25-5.42, $p=0.011$), (3) anemia (COR 4.508, 95%CI 1.91-10.64, $p=0.001$) (4) having a diagnosis of both HTN and DKD (COR 3.853, 95%CI 1.15-12.96, $p=0.029$), (5) previous diagnosis of GERD (COR 6.655, 95%CI 3.18 -13.91, $p<0.001$), (6) previous intake of antacids (COR 2.622, 95%CI 1.17-5.89, $p=0.020$), (7) being employed (COR 2.332, 95%CI 1.15-4.75, $p=0.020$) (8) alcohol consumption (COR 2.477, 95%CI 1.23-5.01, $p=0.012$), and (9) smoking (COR 2.405, 95%CI 1.19-4.86, $p=0.014$).

Discussion

The pooled prevalence of GERD worldwide is 14%, similar to what was found in this study (13.64%), however, there is great geographic variability.^{2,3,20} Compared to several studies in Asia, Southeast Asia, and the Philippines, there is almost two times the prevalence of GERD in Filipino HD patients.^{3,21,22} In a study by Kawaguchi et al., the reported prevalence of GERD in hemodialysis patients was 24.2% compared to a 16.3% prevalence in the general population.²³ The findings are suggestive that ESRD patients on hemodialysis may have specific risks that predispose them to GERD.

In general, the pathophysiology of GERD primarily involves the gastroesophageal junction (the anti-reflux barrier composed of the lower esophageal sphincter and crural diaphragm) that is poorly functioning, coupled with impaired esophageal clearance as well as alterations in esophageal mucosal integrity.²⁴ Gastrin, a polypeptide hormone, has been found to decrease lower esophageal sphincter pressure and increase the transient lower esophageal sphincter relaxation.²⁵ Patients with impaired kidney function, especially ESRD, have elevated serum gastrin concentrations which can be due to impaired degradation and reduced excretion. The basal serum gastrin concentration was inversely related to the basal, maximal, and peak acid output in CRF patients with severe impairment of renal function.²⁶⁻³⁰ In addition,

Table IV. Factors associated with GERDQ ≥ 8 among patients (n=264)

Parameter	Crude Odds Ratio (95% CI)	P-value
Age	1.003 (0.98–1.03)	0.814
Sex		
Male	1.0 (Reference)	-
Female	0.922 (0.46–1.86)	0.820
With Employment	2.332 (1.15–4.75)	0.020
Comorbidities		
Hypertension	0.709 (0.33–1.52)	0.375
Diabetes Mellitus	1.867 (0.91–3.83)	0.088
Chronic Heart Disease	4.041 (1.89–8.64)	<0.001
Cerebrovascular Disease	1.181 (0.44–3.16)	0.741
Anemia	4.508 (1.91–10.64)	0.001
Chronic Lung Disease	2.14 (0.49–9.36)	0.312
Cancer	6.408 (0.65–63.32)	0.112
Gout	1.674 (0.4–7.06)	0.483
Previously Diagnosed with GERD	6.655 (3.18–13.91)	<0.001
Previously took Antacid ^a	2.622 (1.17–5.89)	0.020
Maintenance Medications		
ACE Inhibitor	2.078 (0.08–51.98)	0.656
Angiotensin Receptor Blocker	1.189 (0.59–2.39)	0.626
Alpha Adrenergic Agonist	1.191 (0.58–2.46)	0.636
Beta-Blocker	1.028 (0.45–2.35)	0.948
Calcium Channel Blocker	1.003 (0.5–2.01)	0.993
Diuretics	1.685 (0.61–4.62)	0.311
Iron Supplement	0.243 (0.1–0.61)	0.003
Sodium Bicarbonate	0.642 (0.3–1.35)	0.243
Calcium Carbonate	1.033 (0.48–2.23)	0.934
Erythropoietin Injection	0.561 (0.19–1.69)	0.305
Antiplatelet	1.272 (0.55–2.93)	0.572
Anticoagulant	3.615 (0.74–17.68)	0.112
Insulin	2.599 (1.25–5.42)	0.011
Oral Antidiabetic	1.140 (0.5–2.61)	0.758
Nitrates	3.615 (0.74–17.68)	0.112
Statin	1.495 (0.74–3.04)	0.266
Alcohol consumption	2.477 (1.23–5.01)	0.012
Smoking	2.405 (1.19–4.86)	0.014
Diagnosis		
Congenital kidney disease	1.126 (0.05–25.35)	0.94
Diabetic Kidney Disease	1.0 (Reference)	-
Glomerulonephritis	0.412 (0.07–2.48)	0.333
Gouty nephropathy	1.877 (0.47–7.56)	0.375
Hepatorenal syndrome	1.877 (0.07–49.6)	0.706
Hypertensive Kidney Disease	0.732 (0.3–1.77)	0.488
Hypertensive and Diabetic Kidney Disease	3.853 (1.15–12.96)	0.029
Leptospirosis	1.126 (0.05–25.35)	0.94
NSAID induced Nephropathy	1.877 (0.47–7.56)	0.375
Polycystic Kidney Disease	0.331 (0.02–6.23)	0.461
Post obstructive uropathy	1.126 (0.05–25.35)	0.94
Years in dialysis	1.079 (0.91–1.27)	0.366
Type of vascular access		
AV fistula	1.0 (Reference)	-
Intrajugular	1.279 (0.48–3.44)	0.626
Heparin Use	1.133 (0.06–22.39)	0.935
Frequency per week		
1	1.0 (Reference)	-
2	1.176 (0.06–22.51)	0.914
3	3 (0.15–59.72)	0.472
Duration, hours	0.765 (0.27–2.17)	0.615
Blood flow rate, ml/min	0.998 (0.99–1.01)	0.622
Dialysate Flow Rate, ml/min	0.999 (0.99–1)	0.597
Dialysis Modality		
Conventional	1.0 (Reference)	-
Sequential	19.31 (0.77–483.33)	0.072

a Such as but not limited to H₂-receptor antagonist, Proton pump inhibitors, Aluminum/magnesium tablets, or Alginates
Statistical test used: Firth logistic regression

after HD.^{31–33} Esophageal motility disorders and delayed gastric emptying may also play a role in the development of GERD in ESRD patients owing to altered myoelectric activity, or perhaps to an increased production of gastric acid.³⁴ It has been demonstrated that uremic patients undergoing HD had gastric dysrhythmias during HD that eventually deteriorated after HD, although autonomic neuropathy may be a confounder.³⁵ Delayed gastric emptying usually occurs, especially if both parasympathetic and sympathetic neuropathies are present.³⁶

GERD is associated with various factors. The relationship between CKD and cardiovascular disease remains a complex one.^{37,38} In this study, we found out that having CHD as a comorbidity was four times more likely to have GERD, which is consistent in other observational studies noting about twice more in patients with CHD than in the general population. One plausible explanation is the adverse effect of drugs used in cardiac diseases such as Aspirin; however, no statistical significance was noted in this study. Potential explanations include esophageal-cardiac reflex, autonomic nervous systems disturbances, and visceral pain perception threshold.^{3,39}

Another factor associated with having a GERDQ score of at least eight in HD patients was being on insulin therapy, although there was no statistical difference with having Type 2 diabetes mellitus itself. In some studies, they were able to determine that there is actually an association between GERD and Type 2 diabetes mellitus.^{40,41} The variation may be due to the duration and severity of diabetes mellitus in CKD patients on HD, whereby the duration and quality of diabetes control may have influenced the incidence of GERD, which was found to be inversely related to glycemic control, but this needs to be further verified.^{42, 43}

GERD patients with more severe initial symptoms are more likely to have recurrence. In a study done in Taiwan, the recurrence rate was 30.4%, and it was found out that patients who have a GERDQ score of more than 8 had a significantly higher incidence of recurrence which could independently predict recurrence within one year of follow up.⁴⁴ In our study, 21 of 60 patients were previously diagnosed and treated as GERD, implicating a 35% recurrence rate, and found to have a GERDQ score of 8 and above. This subset of patients comprised 58% of the current GERD positive group. Furthermore, this study found out that having a GERDQ score of eight and above in HD, a previous diagnosis of GERD is six times

patients even while on HD were found to have elevated gastrin levels and the values are the same, before and

more likely, and previous intake of antacids such as proton pump inhibitors was about three times. Although Proton pump inhibitors are effective in the management of GERD, many patients actually relapse after discontinuation.⁴⁵⁻⁴⁶ Additionally, several studies have demonstrated that up to 26-48% of GERD patients had recurrence after 4-8 weeks of Proton pump inhibitor therapy.⁴⁷⁻⁴⁸ Our study showed an even higher rate with 77% of patients previously taking medications for GERD such as PPI. However, we failed to identify the timeline of diagnosis and treatment in our study.

Anemia in CKD is a multifactorial process due to relative erythropoietin deficiency, uremia-induced inhibitors of erythropoiesis, shortened erythrocyte survival, and disordered iron homeostasis.⁴⁹ Our study showed anemia at about five times more likely in GERD compared to non-GERD group. On the other hand, anemia has also been associated as an ALARM symptom for GERD requiring further workup to rule out ongoing blood loss attributed to an active malignancy.⁵⁰⁻⁵¹ In view of this, patients who are currently taking an iron supplement were found to be 76% (COR 0.243, 95%CI 0.1-0.61, $p=0.0030$) less likely to have a GERDQ score of 8 and above (Table IV). But then, meta-analysis confirms that iron supplementation is also associated with significant GI-specific side effects which include abdominal pain and heartburn, although is not dose-dependent and did not specifically mention GERD.⁵² This may then be a counterintuitive finding, and there may be reverse causality; such that those who have had GERD symptoms previously have already stopped iron supplements before the survey. Furthermore, in a separate study, a significant association between the use of PPI and iron deficiency was shown among patients with and without GERD.⁵³

Interestingly, social factors were also related to the GERD group. Patients, being employed was associated with a higher finding of GERD. Patients with GERD were found to have high occupational stress scores and low quality of life. HD patients who faced the possibility of having to stop work or studies as well as a change of life plans had the greatest negative impact on their quality of life.^{54,55} Smoking and alcohol consumption were also independently associated with increased prevalence of GERDQ score of eight or more and are consistent with a recent meta-analysis of 102 articles.³

In this study, we found no statistical difference with regards to the HD profile of our patients such as the modality, duration, frequency, type of vascular access, blood and dialysate flow rate, and the years on HD.

One limitation of the study is that patients may have had recall biases, especially regarding their previous diagnosis of GERD. Moreover, these dialysis patients have multiple comorbidities and are on polypharmacy; hence may have missed out some of the relevant details.

Furthermore, GERD has great geographical variability. Although this study was done in several medical centers, the study was conducted in a single locality, hence may not be representative of other areas. Our sample size

was small and along with the cross-sectional design could limit the conclusions which can be drawn. Further larger scale studies are recommended to look into this to confirm our findings.

In addition, the true prevalence of GERD in HD may be further evaluated using other diagnostic modalities such as endoscopy or 24-pH monitoring. Patients may also be followed up after treatment of GERD to validate the diagnosis.

Conclusion

The prevalence of GERD in Filipino hemodialysis patients according to our results is 13.64% and may be associated with several clinical factors such as heart disease, insulin use, anemia, hypertensive and diabetic kidney disease, previous diagnosis of GERD, use of antacids, currently employed, smoking, and alcohol use. A comprehensive understanding of relationships between these clinical factors could be elucidated further in a larger number of patients.

Conflict of Interest. The authors declare no conflicts of interest.

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Appendix A: GERDQ Filipino Version



Mangyari pong pag-usapan ninyo ng inyong doktor kung paano nakakaapekto ang GERD sa inyong buhay.

Pangalan _____

Petsa _____

Pakisagutan po ang mga sumusunod na tanong. Ang inyo pong mga sagot ay makakatulong sa doktor na malaman ang pinakamabuting paggamot para matiyak na magbabalik sa normal ang inyong buhay.

Balikan ang nakaraang 7 araw

GerDQ

Tsekan (✓) po lamang ang isang kahon kada tanong

Symptom Questions

Nagkakaiba ang sintomas sa bawat tao

A

1. Sa nakaraang isang linggo, ilang araw po kayo nakaramdam ng panakit/panghahapdi ng dibdib (heartburn)?
2. Sa nakaraang isang linggo, ilang araw po kayo nakaranas ng pagbalik o pag-akyat ng laman ng tiyan (likido o pagkain) hanggang sa inyong bibig/lalamunan (regurgitation)?

1.	0 ARAW	1 ARAW	2-3 ARAW	4-7 ARAW	Kabuuang Puntos	<input type="text"/>
	0Pt	1Pt	2Pts	3Pts		
2.	0 ARAW	1 ARAW	2-3 ARAW	4-7 ARAW		
	0	1	2-3	4-7		
	ARAW	ARAW	ARAW	ARAW		

+



B

1. Sa nakaraang isang linggo, ilang araw po sumakit ang inyong sikmura?
2. Sa nakaraang isang linggo, ilang araw po kayo nakaramdam ng parang masusuka?

1.	0 ARAW	1 ARAW	2-3 ARAW	4-7 ARAW	Kabuuang Puntos	<input type="text"/>
	3Pts	2Pts	1Pt	0Pt		
2.	0 ARAW	1 ARAW	2-3 ARAW	4-7 ARAW		
	0	1	2-3	4-7		
	ARAW	ARAW	ARAW	ARAW		

+

Impact Questions

Importante po na maunawaan ng inyong doktor kung paano naapektuhan ng inyong sintomas ang pang-araw-araw ninyong buhay

C

1. Sa nakaraang isang linggo, ilang araw po kayo hindi makatulog o nagigising dahil sa panakit/panghahapdi ng dibdib at/o pag-akyat/pagbalik ng laman ng tiyan (likido o pagkain) hanggang sa inyong bibig/lalamunan?
2. Sa nakaraang isang linggo, ilang araw po kayo gumamit ng karagdagang gamot maliban sa inireseta ng inyong doktor para sa panakit/panghahapdi ng dibdib at/o pag-akyat/pagbalik ng laman ng tiyan (likido o kinain) hanggang sa inyong bibig/lalamunan?

1.	0 ARAW	1 ARAW	2-3 ARAW	4-7 ARAW	Kabuuang Puntos	<input type="text"/>
	0Pt	1Pt	2Pts	3Pts		
2.	0 ARAW	1 ARAW	2-3 ARAW	4-7 ARAW		
	0	1	2-3	4-7		
	ARAW	ARAW	ARAW	ARAW		

=

Puntos

Ang GerDQ po ay dresenyo para makatulong sa pagtukoy ng mga pasyenteng may GERD at masubaybayan ang kanilang puggalang. Hindi po ito ginawa para palitan ang payo ng doktor. Makabubuti po na laging kumonsulta sa inyong doktor.