Association of Protein-Energy Wasting and Oxidative Stress Markers in Peritoneal Dialysis

Francisco Gerardo Yanowsky-Escatell,[1,2] Leonardo Pazarín-Villaseñor,[1,3*] Jorge Andrade-Sierra,[4] Yessica García-Salas,[1] Andrés García-Sánchez,[4] Alejandra Guillermina Miranda-Díaz,[4] Tonatiuh Delgado-Figueroa,[1] Pedro Alberto Mendoza-Rosales,[1] Eduardo de Jesús Torres-Vázquez,[1] Carlos Alberto Andrade-Castellanos,[1] María Teresa Tapia-de-la-Paz,[1] Diana Mercedes Hernández-Corona,[5] Tonatiuh González-Heredia,[5] Kevin Javier Arellano-Arteaga,[1] Luis Miguel Román-Pintos[2]

[1]Department of Internal Medicine, Civil Hospital of Guadalajara Dr. Juan I. Menchaca, Guadalajara, Jalisco, Mexico
[2]Department of Health Sciences-Illness as an Individual Process, University Center of Tonala, University of Guadalajara, Guadalajara, Jalisco, Mexico
[3]University of Guadalajara, University Center for Health Sciences, Specialty in Nephrology. Regional General Hospital No. 46 IMSS, Guadalajara, Jalisco, Mexico
[4]Department of Physiology, University Health Sciences Center, University of Guadalajara, Guadalajara, Jalisco, Mexico
[5]Multidisciplinary Health Research Center, Biomedical Science Department, University Center of Tonala, University of Guadalajara, Guadalajara, Jalisco, Mexico

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Introduction. Protein-energy wasting (PEW) is highly prevalent among patients undergoing peritoneal dialysis (PD), and it has been proposed that oxidative stress (OS) may contribute to its pathogenesis. This study was an attempt to determine the association between the presence of PEW and OS levels in PD patients.
Methods. This analytical cross-sectional study involved 62 clinically stable PD patients aged ≥ 18 years, between September 2017 and July 2018. PEW was assessed using PEW definition criteria, 7-point Subjective Global Assessment (SGA), and Malnutrition-Inflammation Score (MIS). Redox state was evaluated through oxidants (lipoperoxides, 8-Isoprostane, nitric oxide), antioxidants (superoxide dismutase, catalase, glutathione peroxidase-GPx, total antioxidant capacity), and oxidative DNA damage [8-hydroxy2′-deoxyguanosine-8-OHdG, 8-Oxoguanine-DNA-N-Glycosylase-1(8-OHdG)].
Results. Among study participants, 38 (61.2%) were males and 24 (38.8%) were females; 22 (35.4%) had diabetes mellitus [males 15 (68.1%) and females 7 (31.8%)]. The average PD duration was 11 (4-27) months, body mass index: 23.5 ± 4.1 kg/m2, energy intake: 1138.4 ± 394.2 kcal/day, and protein intake: 50.2 ± 18.5 g/day. Prevalence of PEW varied based on the assessment method used (50-88.7%). Plasma 8-OHdG levels were higher in patients with PEW evaluated by MIS (0.1 [0.1-56.4] vs. 1.8 [0.1-74.7] ng/mL, P = .028), while GPx activity was lower in the presence of PEW as measured by MIS (3.6 [3.1-7.6] vs. 2.8 [1.2-10] nmol/min/mL, P = .021). No significant differences were observed between PEW markers and remaining OS levels.
Conclusions. In PD patients with PEW, assessed by MIS, 8-OHdG was significantly increased, while GPx activity was significantly low.

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INTRODUCTION

End-stage kidney disease (ESKD) poses a significant public health challenge in Mexico.[1] Data from the United States Renal Data System (USRDS) indicate that the region of Jalisco, Mexico, exhibits one of the highest incidence rates of treated ESKD

and peritoneal dialysis (PD) utilization.[2]

Oxidative stress (OS) has emerged as a potential contributor to morbidity and mortality in ESKD patients, playing a pivotal role in the pathogenesis of atherosclerosis. [3] OS is defined as an imbalance between oxidants and antioxidants, favoring oxidants;[4] this imbalance leads to damage to macromolecules such as DNA, proteins, carbohydrates, and lipids.[5]

Patients undergoing PD experience increased oxidative stress due to the use of standard PD solutions, which results in the development of advanced glycation end products and reactive oxygen species.[6] Elevated OS levels are evident in the early stages of chronic kidney disease (CKD), escalating with the progression to ESKD. Factors such as inflammation, uremic toxins, fluid overload, anemia, and dialysis contribute to the production of free radical, reactive oxygen species, and a decrease in the antioxidant system.[7]

In pathological conditions, the interaction between pro-oxidant agents (reactive oxygen/nitrogen species) and antioxidants (superoxide dismutase-SOD, glutathione peroxidase-GPx, catalase) activates enzymatic and non-enzymatic antioxidant defense mechanisms to counteract the deleterious effects of radicals on the systems.[8] Notably, SOD and GPx activity are markedly reduced in PD patients, and some studies suggest an elevated level of OS in these individuals.[9,10]

Protein-energy wasting (PEW) is a common complication in ESKD patients,[11] characterized by a decline in body protein and fat mass due to multiple nutritional and catabolic alterations.[12,13] Among PD populations, PEW is highly prevalent (32-49%),[14] exhibiting a serious problem, as it is associated with worse outcomes in these patients.[15.16]

The assessment of nutritional status is crucial for detecting and managing PEW, with widely recommended tools such as the PEW-definition criteria, Subjective Global Assessment (SGA), and Malnutrition-Inflammation Score (MIS).[17] OS may contribute to the pathogenesis of PEW in ESKD patients.[18-21] However, data on which PEW markers affect OS in PD patients are lacking. Therefore, this study was an attempt to determine the association between the presence of PEW, as evaluated by PEW-Definition Criteria, SGA, and MIS, with OS levels in these patients.

MATERIALS AND METHODS

An analytical cross-sectional study was conducted from September 2017 to July 2018, involving 62 clinically stable PD or patients 38 (61.2%) were males and 24 (38.8%) were females), aged ≥18 years, who were undergoing continuous ambulatory PD with duration 11 (4-27) months. The participants were recruited from the Nephrology Service of the Hospital Civil de Guadalajara Dr. Juan I. Menchaca, located in Guadalajara, Jalisco, Mexico.

Exclusion criteria comprised clinical or biochemical evidence of any infectious process (such as peritonitis, urosepsis, soft tissue infection, or pneumonia) within the previous month, systemic inflammatory diseases (including cancer, systemic lupus erythematosus, vasculitis, or other connective tissue diseases), onset of PD less than one month before the study period, and who denied their consent to participate in the study.

The study adhered to the principles outlined in the Declaration of Helsinki and followed ethical guidelines for medical research involving human participants. The research protocol received approval from the Ministry of Health of Jalisco, Department of Institutional Development (with State Research Registry number 0182/17 HCJM/2017), and all participating patients provided written, informed consent.

Biochemical data

Biochemical data, including hemoglobin, total lymphocyte count, glucose, creatinine, urea, blood urea nitrogen (BUN), albumin, total protein, cholesterol, and transferrin, were obtained minutes before the nutritional evaluation of patients. These measurements were conducted in the hospital's clinical laboratory. Similarly, OS markers were collected in the same manner, preceding the nutritional evaluation.

Oxidants

Lipoperoxides (LPO)

Plasma levels of LPO were measured using the FR22 assay kit (Oxford Biomedical Research Inc., Oxford, MI, USA®). The chromogenic reagent reacts with malondialdehyde (MDA) and 4-hydroxy-alkenals, forming a stable chromophore. A pattern curve with known concentrations of 1,1,3,3-Tetramethoxypropane in Tris-HCl was employed.

8-Isoprostane (8-IP)

The immunoassay reagent kit from Abcam Company® (Cambridge, USA) was utilized following the manufacturer's instructions. The 8-IP assay was based on the principle of competitive binding using a maximum binding control, and absorbance was read at 450 nm.

Nitric Oxide (NO)

A colorimetric method, as per the kit (NB98, Oxford Biochemical, Oxford, MI, USA®), was employed for the determination of NO. Standard or sample (85 µL) was added to plate wells, along with 10 µL of nitrate reductase and 10 µL of 2 mM NADH. The plate was stirred for 20 minutes at room temperature, and absorbance at 540 nm was read within the first 20 minutes.

Antioxidants

Superoxide Dismutase

The detection of O2 generated by the enzymes xanthine oxidase and hypoxanthine was performed using the kit manufacturer's instructions (SOD No. 706002, Cayman Chemical Company®, USA). Absorbance was read at 440 nm.

Glutathione Peroxidase

The Glutathione Assay Kit (No. 703102, Cayman Chemicals®, USA) was used to measure GPx activity indirectly by a coupled kinetic reaction with glutathione reductase. The decrease in absorbance due to the oxidation of nicotinamide adenine dinucleotide phosphate (NADPH) was measured at 340 nm every minute.

Catalase

Catalase was determined using the Bioxytech Catalase-520® kit per manufacturer's instructions (cat. 21042, OXIS Int, Beverly Hills, CA, USA®). Absorbance was read at 520 nm.

Total Antioxidant Capacity (TAC)

TAC evaluations were conducted following the kit manufacturer's instructions (Total Antioxidant Power Kit, No. TA02.090130, Oxford Biomedical Research®). The dilution factor was considered in the result.

Oxidative DNA Damage

8-hydroxy2'-deoxyguanosine (8-OHdG)

Serum levels of 8-OHdG were measured using the 8-hydroxy-2-deoxyguanosine ELISA kit ab201734 (Abcam®, Cambridge, MA, USA). Tetramethylbenzidine (TMB) substrate was utilized to obtain a color signal measured at 450 nm.

8-Oxoguanine-DNA-N-Glycosylase-1 (hOGG1)

This was performed using the MyBioSource® human 8-oxoguanina-DNA-N- glycosidase ELISA kit no. MBS702793, employing a sandwich ELISA. A color signal was obtained by adding TMB substrate, and color development was measured at 450 nm.

Anthropometric Parameters

Anthropometric measurements included body weight, height, biceps skinfold thickness (BSF), triceps skinfold thickness (TSF), and mid-arm circumference (MAC). Mid-arm muscle circumference (MAMC) was calculated based on MAC and TSF[22]. MAMC values were compared with the 50th percentile of the reference population[23] and adjusted to be considered as a reduction in muscle mass. BSF and TSF were used to estimate the percentage of body fat (%BF).[24,25]

Dietary Intake

Dietary intake was determined by a 24-hour recall based on the Equivalent Food System for Kidney Patients.[26] For energy and protein adjustment, the ideal weight was used (ideal body weight = [BMI = 23 kg/m^2] × height^2).

Assessment of Protein-Energy Wasting

Protein-Energy Wasting Definition Criteria

According to the 4 categories proposed by the International Society of Renal Nutrition and Metabolism (ISRNM), PEW[12] was diagnosed when at least one of the following criteria was met: serum albumin < 3.8 g/dL or cholesterol < 100 mg/dL for serum chemistry, BMI < 23 kg/m^2, unintentional loss of 5-10% of weight, total body fat percentage < 10% for body mass, reduced MAMC for muscle mass, and dietary protein intake < 0.80 g/kg/day, or dietary energy intake of < 25 kcal/kg/day for dietary intake.

Subjective Global Assessment (SGA)

The 7-point SGA is based on two major categories: medical history and physical examination. Once this examination is completed, an overall SGA rating is assigned to the patient, ranging from a rating of 1–2 for severe PEW, 3–5 for mild-moderate PEW, and 6–7 for well-nourished.[27-28] In this study, SGA scores ≤5 were considered indicative of the presence of PEW.

Malnutrition-Inflammation Score (MIS)

The MIS utilizes a revised form of the SGA scoring system. Each component presents four levels of severity from 0 (normal) to 3 (severely abnormal). The sum of all 10 MIS components ranges from 0 (normal) to 30 (severe PEW), and a higher score reflects a more severe degree of PEW and inflammation.[27-29] A score ≥ 6 was considered indicative of the presence of PEW.[30]

Statistical Analysis

The Kolmogorov-Smirnov test was used to determine the distribution of dimensional variables, presented as mean ± standard deviation or median (25-75%), as appropriate, and nominal variables were expressed as numbers and percentages. For differences among groups, Student's t-test and U Mann-Whitney tests were applied according to variable type. We performed a multivariate logistic regression analysis adjusted for OS variables to determine factors associated with PEW criteria in PD patients. The variables included in these models were those that showed statistical significance in the bivariate analysis, and adjusted Odds Ratios (OR) and their 95% Confidence Intervals (95% CIs) were obtained as risk measures in these models using the stepwise method. All statistical calculations were conducted with SPSS version 21 software (SPSS, Inc., Chicago, IL). A $P < .05$ was considered significant.

RESULTS

A total of 62 patients were assessed, comprising 38 men (61.3%), 24 women (38.7%), and 22 individuals (35.4%) diagnosed with diabetes [males 15 (68.1%) and females 7 (31.8%)]. The average duration of PD was 11 (4-27) months. The average Body Mass Index (BMI) was 23.5 ± 4.1 kg/m^2. Energy intake averaged 1138.4 ± 394.2 kcal/day with 18.7 ± 5.9 kcal/kg/day, while protein intake was 50.2 ± 18.5 g/day with 0.8 ± 0.2 g/kg/day. The prevalence of PEW varied depending on the assessment method used: PEW-definition criteria (67.7%), PEW-7-point SGA ≤ 5 (50%), and PEW-Malnutrition-Inflammation Score (MIS) ≥ 6 (88.7%). Regarding biochemical data, albumin levels were 2.7 ± 0.4 g/dL, cholesterol levels were 167.9 ± 44.4 mg/dL, and transferrin levels were 179.1 ± 3 mg/dL. Table 1 provides additional patient characteristics.

Table 1. Characteristics of peritoneal dialysis patients.

	N=62
Gender	
Male n (%)	38 (61.3)
Female n (%)	24 (38.7)
Age (years)	37.3 ± 15.6
Male (years)	38.1 ± 15.5
Female (years)	36 ± 16.1
Diabetics (%)	22 (35.4)
Time on PD (months)	11 (4-27)
Anthropometrics parameters	
Weight (kg)	62.4 ± 13.8
Height (cm)	162.3 ± 10.2
BMI (kg/m^2)	23.5 ± 4.1
MAC (cm)	26.9 ± 4.2
BST (mm)	5 (1.50-20)
TST (mm)	10.9 ± 5.7
MAMC (cm)	23.5 ± 3.1
Percentage of body fat (%)	22.4 ± 8.0
Dietary intake	
Energy intake (kcal/day)	1138.4 ± 394.2
Energy intake per body weight (kcal/kg/day)	18.7 ± 5.9
Protein intake (g/day)	50.2 ± 18.5
Protein intake per body weight (g/kg/day)	0.8 ± 0.2
Assessment PEW	
PEW-Definition Criteria n (%)	42 (67.7)
SGA mean score (sd)	5.5 ± 0.7
PEW-SGA ≤ 5 n (%)	31 (50)
MIS mean score (sd)	10.4 ± 3.8
PEW-MIS ≥ 6 n (%)	55 (88.7)
Laboratory parameters	
Hemoglobin (g/dL)	9.6 ± 2.0
Total lymphocyte count (cells/mm^3)	1740 ± 678.9
Glucose (mg/dL)	87.50 (62-225)
Creatinine (mg/dL)	10.2 ± 3.7
Urea (mg/dL)	113.5 ± 41.5
BUN (mg/dL)	53.2 ± 19.2
Albumin (g/dL)	2.7 ± 0.4
Total proteins (g/dL)	5.7 ± 0.6
Cholesterol (mg/dL)	167.9 ± 44.4
Transferrin (mg/dL)	179.1 ± 3

PD, Peritoneal dialysis; BMI, Body mass index; MAC, Mid-arm circumference; BST, Biceps skinfold thickness; TST, Triceps skinfold thickness; MAMC, Mid-arm muscle circumference; PEW, Protein-energy wasting; SGA, Subjective global assessment; MIS, Malnutrition-inflammation score.

Protein-Energy Wasting and Oxidants

No differences were observed between PEW markers and levels of oxidants, including LPO, 8-IP, and NO (Table 2).

Protein-Energy Wasting, Antioxidants, and Total Antioxidant Capacity

Regarding the evaluation of various antioxidant parameters, the plasma levels of GPx, an enzyme that plays a key role in antioxidant defense

Table 2. Markers of oxidants, antioxidants, and oxidative DNA damage in patients without and with PEW.

	Without PEW-Definition Criteria	With PEW-Definition Criteria	*P*	Without PEW-SGA 6-7	With PEW-SGA ≤ 5	*P*	Without PEW-MIS 0-5	With PEW-MIS ≥ 6	*P*
Oxidants									
LPO (micromol/L)	3.7 ± 0.8	3.8 ± 0.9	0.748	4 ± 0.9	3.6 ± 0.9	0.068	3.7 ± 0.5	3.8 ± 0.9	0.826
8-IP (pg/mL)	26 ± 5.9	26 ± 7.5	0.944	25.2 ± 6.3	26.8 ± 7.7	0.322	24.8 ± 4.8	26.1 ± 7.3	0.669
NO (mM)	202.7 ± 119.8	220.6 ± 100.3	0.764	237.8 ± 98.4	192.6 ± 109.7	0.177	250.7 ± 102.5	210.5 ± 106.3	0.390
Antioxidants									
SOD (U/mL)	0.3 ± 0.1	0.3 ± 0.1	0.481	0.3 ± 0.1	0.3 ± 0.1	0.531	0.2 ± 0.1	0.3 ± 0.1	0.58
GPx (nmol/min/mL)	3.3 (1.4-7.6)	2.8 (1.2-10)	0.133	3.1 (1.4- 10)	2.7 (1.2-7)	0.439	3.6 (3.1-7.6)	2.8 (1.2-10)	0.021*†
Catalase (mM)	20 ± 0.6	20.3 ± 1	0.227	20.1 ± 0.6	20.3 ± 1.1	0.260	20 ± 0.8	20.3 ± 0.9	0.462
TAC (mM)	2.7 ± 0.4	2.5 ± 0.5	0.329	2.6 ± 0.4	2.5 ± 0.5	0.680	2.7 ± 0.3	2.5 ± 0.5	0.352
Oxidative DNA Damage									
8-OHdG (ng/mL)	0.6 (0.1-73)	2.3 (0.1-74.7)	0.358	1.7 (0.1-74.7)	1 (0.1-74.1)	0.341	0.1 (0.1-56.4)	1.8 (0.1-74.7)	0.028*†
hOGG1 (ng/mL)	0.04 (0-1.8)	0.04 (0-0.05)	0.734	0.04 (0.01-1.8)	0.03 (0-0.04)	0.243	0.04 (0.04-0.05)	0.04 (0-1.8)	0.659

*GPx, and 8-OHdG values expressed on median (interquartile rank) between patients with and without PEW evaluated with MIS
† $P < 0.05$ U Mann Whitney
PEW, Protein-energy wasting; SGA, Subjective global assessment; MIS, Malnutrition-inflammation score.
LPO, lipoperoxides; 8-IP, 8-Isoprostane NO, nitric oxide; SOD, superoxide dismutase; GPx, glutathione peroxidase; TAC, total antioxidant capacity; 8-OHdG, 8-hydroxy2'-deoxyguanosine; hOGG1, 8-Oxoguanine-DNA-N-Glycosylase.

mechanisms, were lower in the group of patients with PEW as evaluated by MIS (3.6 [3.1-7.6] vs 2.8 [1.2-10] nmol/min/mL, *P* = .021). However, these differences were not observed with the rest of the antioxidants evaluated by MIS. The levels of SOD, catalase, and TAC did not differ based on PEW-Definition Criteria and 7-point SGA (Table 2).

Protein-Energy Wasting and Oxidative DNA Damage

Oxidative DNA damage, as measured by the 8-OHdG level, was significantly higher in the MIS group (0.1 [0.1-56.4] vs 1.8 [0.1-74.7] ng/mL, *P* = .028). There was no change in the repair enzyme for oxidatively damaged DNA (hOGG1) between groups (Table 2).

Diagnostic Criteria for PEW, MAMC, Protein Intake, Weight Loss, Percentage of Body Fat, and Cholesterol

According to the diagnostic criteria for PEW and OS parameters, significantly lower levels of GPx [2.41 (1.27-7) vs 3.31 (1.40-10.06) nmol/min/mL, *P* = .008] were found in the reduced MAMC group. Meanwhile, for the low protein intake group, higher levels of catalase (20.36 ± 0.90 vs 19.70 ± 0.63 mM, *P* = .041) were observed, along with elevated levels of 8-isoprostanes (31.05 ± 8.82 vs 24.47 ± 5.62 pg/mL, *P* = .001) in the greater weight loss group. As for the low percentage of body fat group, higher levels of 8-OHdG [74.41 (74.12-74.70) vs 1.05 (0.15-74.58) ng/mL, *P* = .002] were found. Additionally, for the diagnostic criteria of low cholesterol, higher levels of catalase (22.09 vs 20.23 ± 0.87 mM, *P* = .040) were observed.

The rest of the diagnostic criteria, caloric intake, and body mass index showed no significant differences with oxidative stress parameters.

Multivariable Logistic Regression Analysis to Identify the Risk Factors for Criteria PEW in PD

When conducting a multivariate analysis with MAMC as the dependent variable, and adjusting for catalase, 8-IP, 8-OHdG, GPx (OR = 1.649, 95% CI: 1.083-2.510, *P* = .020) remained an associated factor with MAMC. In the multivariate analysis for protein intake, adjusted for GPx, 8-IP, and 8-OHdG, catalase (OR = 0.184, 95% CI: 0.045-0.757, *P* = .019) remained an associated factor with protein intake. Lastly, in the multivariate analysis

Table 3. Associated factors with criteria PEW in PD.

	Univariate intro method			Multivariate Stepwise method		
	OR	95% CI	*P*	OR	95% CI	*P*
Associated factors with MAMC						
GPx	1.655	1.081-2.535	0.020	1.649	1.083-2.510	0.020
Catalase	1.038	0.570-1.889	0.903	----	----	---
8-IP	0.996	0.924-1.074	0.926	----	----	----
8-OHdG	0.997	0.981-1.013	0.712	----	----	----
Associated factors with protein intake						
Catalase	0.073	0.009-0.598	0.015	0.184	0.045-0.757	0.019
GPx	0.966	0.543-1.718	0.906	----	----	----
8-IP	0.845	0.701-1.018	0.076	----	----	----
8-OHdG	0.982	0.954-1.010	0.204	----	----	----
Associated factors with weight loss						
8-IP	0.864	0.778-0.961	0.007	0.873	0.791-0.963	0.007
GPx	0.756	0.522-1.095	0.139	----	----	----
Catalase	0.595	0.306-1.158	0.126	----	----	----
8-OHdG	0.993	0.973-1.014	0.520	----	----	----

Multivariable logistic regression analysis. Dependent variable presence of criteria of PEW in PD. OR: odds ratios; 95% CI: 95% confidence intervals. Crude ORs were obtained using the Enter method. Ajusted ORs were obtained using the Forward stepwise method. MAMC: mid-arm muscle circumference; GPx: glutathione peroxidase; 8-Ip: 8-Isoprostane; 8-OHdG: 8-hydroxy2'-deoxyguanosine.

for weight loss, after adjusting for GPx, catalase, and 8-OHdG, 8-IP (OR = 0.873, 95% CI: 0.791-0.963, *P* = .007) continued to be a risk factor associated with weight loss (Table 3).

A bivariate analysis was performed for body fat percentage and cholesterol with 8-IP and 8-OHdG; however, due to the number of patients, it was not possible to conduct a multivariate analysis.

DISCUSSION

The current study investigated OS indicators in clinically stable PD patients and revealed elevated levels of 8-OHdG and reduced GPx activity in the PEW group, as evaluated by the MIS. The levels related to OS, other than 8-OHdG and GPx, were similar, irrespective of the presence or absence of PEW. This increase is believed to be linked with the capability of the MIS tool to not only diagnose PEW but also detect inflammation in CKD patients.[31-34]

One of the main complications in PD patients is the occurrence of PEW and OS. This study reveals a high prevalence of PEW (50-88.7%), which varies based on the detection method employed, in contrast to earlier studies from different regions (32-49%).[14] Various factors contribute to the etiology of PEW, including decreased calorie-protein intake, co-morbid conditions, increased production of inflammatory cytokines, nutrient loss during PD, peritonitis, composition of PD solutions (lactate, pH, etc.), and the onset of OS, are the most important among others.[12,13,35]

In response to the overproduction of reactive oxygen species, various antioxidant defense mechanisms act to counteract them, with GPx being one of the primary enzymes that break down hydrogen peroxides (H_2O_2) to O_2 and lipid peroxides to alcohols.[8] Antioxidant enzymes, including GPx, are notably reduced in ESKD patients, especially those undergoing PD.[10]

Few studies have explored OS parameters in association with PEW in PD patients. In this study, we observed reduced GPx activity in patients with PEW, as evaluated by MIS and a low MAMC. This finding agrees with Çelik *et al.*, who demonstrated an association between antioxidant status (measured by GPx) and nutritional status in hemodialysis patients.[36] However, this association has not been consistently demonstrated in other studies.[37] Similarly, serum ascorbic acid, another plasma antioxidant, does not significantly differ between patient groups with or without PEW, as graded by SGA.[38]

Regarding oxidant biomarkers, we did not observe significant differences using PEW screening tools (PEW-definition criteria, 7-point SGA, MIS). However, other researchers have shown higher levels of malondialdehyde in diabetic patients with PEW, as measured by SGA.[39]

The primary marker of oxidative DNA damage is 8-OHdG.[6] In this study, we observed a significant overexpression of this parameter in PEW patients as evaluated by MIS. However, this finding cannot be corroborated in our PD patients. In hemodialysis patients, 8-OHdG does not significantly differ between well-nourished individuals and those with PEW.[40]

A low dietary intake was observed in most PD patients. In the evaluation of PEW, dietary intake is considered one of the crucial categories and has been proposed as one of the main tools to assess it.[12]

We found that catalase levels are associated with protein intake. This finding has not been previously described in PD but has been observed in a study involving hemodialysis patients, which demonstrated that the determination of plasma thiols (cysteinylated protein, cystine, protein thiolation index) is inversely associated with energy and protein intake.[41] This finding is significant, as it is postulated that in the ESKD population, spontaneous nutritional intake is linked to OS and, in turn, contributes to PEW. However, the isolated evaluation of dietary intake is not considered an independent marker for diagnosing PEW, as per recommendations, since it is necessary to complement it with other categories that encompass the loss of muscle mass and fat mass, or other biochemical parameters, among others.[12,28,29]

The available evidence indicates a significant association between OS and cardiovascular mortality in this patient group. OS, as a primary disturbance, leads to inflammation, which in turn exacerbates OS. Similarly, inflammation, as a primary disturbance, can induce OS and worsen it.[34]

Lastly, some findings suggest that OS induces protein breakdown and muscular atrophy.[42-44] Therefore, the observed increase in 8-OHdG and decreased GPx activity in the present study may be a response to the pathological condition of PEW evaluated with the MIS. This alteration in the redox state confers greater systemic inflammation, which, in turn, worsens OS parameters.[45,46] Thus, OS and inflammation may induce PEW through protein degradation pathways such as the ubiquitin-proteasome system, autophagy-lysosome pathway, calpain and caspase pathways, insulin-like growth factor-1 pathway, and myostatin, among others,[47,48] which are still under investigation in chronic disease conditions.

Limitations

The main limitations of this study include the small sample size, making it challenging to replicate in other populations. Additionally, due to the cross-sectional nature of the study, it was not possible to assess changes in OS and PEW parameters over time. Finally, inflammatory markers such as interleukin-6, tumor necrosis factor-alpha, and C-reactive protein were not evaluated, although these markers are commonly used to assess the inflammatory state in various conditions. Nevertheless, we believe that these limitations do not affect the results of this study, given that the patients were stable, without indicators of infection or previously diagnosed autoimmune conditions, thus not affecting the redox state at the time of their evaluation.

CONCLUSIONS

In conclusion, we observed a significant increase in 8-OHdG and decreased GPx activity in clinically stable PD patients diagnosed with PEW, as evaluated by the MIS tool. Additionally, we observed that the remaining OS parameters did not differ with or without the presence of PEW using other recommended tools (PEW-Definition Criteria, 7-point Subjective Global Assessment, MIS).

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose.

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None.

CODE OF CONDUCT

We follow the World Health Organization (WHO) code of conduct for this research.

ETHICAL CONSIDERATIONS

The research protocol received approval from the Ministry of Health of Jalisco, Department of Institutional Development (with State Research Registry number 0182/17 HCJM/2017), and all participating patients provided written, informed consent.

GRANTING AGENCY

None.

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*Correspondence to:
Leonardo Pazarín-Villaseñor
University of Guadalajara, University Center for Health Sciences, Specialty in Nephrology. Regional General Hospital No. 46 IMSS, Calzada Lázaro Cárdenas Avenue #2063, 8 de Julio, Zip Code 44910, Guadalajara, Jalisco, Mexico.
E-mail: leopazarin@hotmail.com

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