ORIGINAL ARTICLE

Clinical Profile and Outcomes of Patients with Chronic Kidney Disease on Chronic Hemodialysis Hospitalized for Acute Coronary Syndrome in a Tertiary Public Hospital in the Philippines

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ABSTRACT

Introduction. Acute coronary syndrome (ACS) and end-stage renal disease (ESRD) are both prevalent globally. The diagnosis and management of ACS in ESRD is difficult because the interplay of cardiovascular and renal disease is complicated. The guidelines for ACS may not be applicable to the ESRD population because the trials from which these are drawn mostly excluded ESRD patients.

Objective. To determine the clinical profile and outcomes of CKD patients on dialysis admitted for ACS in the Philippine General Hospital (PGH).

Methods. We did a retrospective cohort study and employed a retrospective review of electronic medical records among ESRD patients presenting with ACS in PGH from May 2021 to November 2023. The collected data was analyzed using univariate and bivariate statistics using PRISM software.

Results. A total of 48 patients with ESRD were admitted for ACS in this study – 8 with STEMI and 40 with NSTEMI. The mean age was 61 years old and 33 (68.8%) were male. Among those with STEMI, six (75%) presented with Kilip II or more. While among those with NSTEMI, 17 (42.5%) had a GRACE score >140 and 27 (67.5%) had an NSTEMI TIMI risk score >2. On average, the patients were on hemodialysis for 31 months prior to admission. The most common comorbidities were hypertension (91.7%) and heart failure (83.3%). On admission, 18 (37.5%) presented with SBP >160, 7 (14.6%) patients presented with shock, and 4 (8.3%) patients presented with cardiac arrest. 38 (79.2%) patients had anemia on admission. 21 (43.8%) patients had left ventricular hypertrophy on electrocardiogram while 34 (70.8%) patients had cardiomegaly on chest radiography. The average left ventricular ejection fraction on echocardiogram was 46% and 27 (90%) patients had segmental wall motion abnormalities. The most common angiographic finding was 3-vessel coronary artery disease seen in 50% of patients. Almost all patients received dual-antiplatelet therapy, high dose statin, and beta-blocker. The mortality rate was high at 43.8% with cardiovascular causes being the most common cause of death.

Conclusion. This study demonstrates the high mortality rate among patients with ESRD presenting with ACS. Our study portrays that patients with ESRD present with higher risk features including abnormalities in vital signs, laboratories, imaging, high prognostications score, and high in-hospital morbidity.

Keywords: end-stage renal disease, chronic kidney disease, acute coronary syndrome, myocardial infarction

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INTRODUCTION

Background of the Study

Ischemic heart disease (IHD) remains to be the top cause of mortality in the Philippines.[1] In the Philippine General Hospital (PGH), acute coronary syndrome (ACS) is among the top 3 causes of mortality among ER patients admitted under the Department of Medicine.[2]

Chronic kidney disease (CKD), on the other hand, is slowly becoming a global public health threat with an estimated prevalence of ~13.4%.[3] It is defined by the KDIGO as abnormalities of kidney structure or function, present for >3 months, with implications for health.[4] In the Philippines, there were a total of 21,535 new patients started on dialysis in 2016.[5] The top three causes of CKD Stage V needing dialysis, or End-Stage Renal Disease (ESRD), in the Philippines are diabetes, hypertension, and chronic glomerulonephritis.[5] While the most common associated comorbidities are diabetes, hypertension, and ischemic heart disease, respectively.[5]. In the PGH Department of Medicine, CKD remains on the list of top reasons for admission.[2]

Of the many risk factors for ACS, CKD remains to be of great concern because the interplay of cardiac and renal disease is inherently complicated.[6,7] Cardiovascular death rates are estimated to be 10–30 times higher in patients undergoing dialysis compared to the general population.[8] Interestingly, the risks associated with experiencing ACS among CKD patients are not fully explained solely by the traditional risk factors of cardiovascular disease such as hypertension, diabetes, and dyslipidemia. Non-traditional risk factors present in patients with CKD such as chronic inflammation, endothelial dysfunction from hyperhomocysteinemia and oxidative stress, and coronary artery calcification from bone-mineral disease, have all been associated with accelerated atherosclerosis, and thereby increasing the occurrence of coronary events.[9] In addition, a phenomenon called platelet reactivity has been described as the blood interacts with hemodialysis membranes, which stimulates platelet aggregation leading to an increased risk of ischemic events and resistance to antithrombotic treatment in dialyzed patients.[10,11]

Currently, there is paucity of data regarding the clinical profile and its association to clinical outcomes among patients who are on chronic hemodialysis and are hospitalized for ACS. Hence this study sought to provide a descriptive and analytic vantage point to better understand the profile of these patients.

Significance of the Study

Historically, ESRD patients, particularly those on maintenance hemodialysis, have been excluded in almost all of the landmark trials concerning the diagnosis and management of ACS.[12] As such, conclusions and recommendations regarding the management of ACS drawn from these studies, which have served as the basis for most major clinical practice guidelines in ACS, may not be as generalizable to the subset of ESRD patients. In fact, there is a growing body of evidence which suggests that the standard treatment modalities for ACS may act differently among patients with CKD especially those on hemodialysis.[7,13,14] Based on several subgroup analysis of several landmark trials in ACS, aspirin still seems to be important in the management of ACS among hemodialysis patients but there is uncertainty regarding the role of other antiplatelets and even statins among these patients.[15]

Moreover, data on ESRD patients on chronic hemodialysis managed using these standards of care in ACS is gravely lacking, particularly in Asia and in the Philippines. Due to these gaps in knowledge, there is a need for a better understanding of clinical profile, risk factors, and outcomes with regard to the diagnosis and management of ACS among ESRD patients on maintenance hemodialysis in order to provide optimal patient care.

As such, this study sought to describe the sociodemographic, clinical, and laboratory profile of this subset of patients in greater depth.

OBJECTIVES

General Objectives

This study aimed to describe and correlate the clinical characteristics and in-hospital outcomes of ESRD patients on chronic hemodialysis hospitalized for acute coronary syndrome in the University of the Philippines - Philippine General Hospital from May 2021 to November 2023.

Specific Objectives

Specifically, this study aimed to determine the following:

- the sociodemographic profile, baseline clinical characteristics, and baseline laboratory and imaging findings
- the type of acute coronary syndrome (non-ST elevation myocardial infarction, ST-elevation myocardial infarction) the patients presented with
- the severity of ACS accordingly (Killip for STEMI and TIMI/GRACE for NSTEMI)
- the medications given to the patients during admission
- the coronary angiographic findings among those who have undergone coronary angiography, their indications for invasive imaging
- the length of stay in the hospital
- the incidence of in-hospital major adverse cardiovascular events, in-hospital non-cardiovascular morbidity, and all-cause mortality
- the risk factors for in-hospital major adverse cardiovascular events and all-cause mortality

REVIEW OF LITERATURE

ACS diagnosis and prognosis in CKD

The interplay between cardiac and renal disease is very complex especially in the diagnosis and management of

ACS. This complexity manifests itself firstly in the ambiguity of the diagnosis of ACS among patients with CKD because it is not that straightforward in this population. The most sensitive and specific biomarker for early diagnosis of ACS is high-sensitivity cardiac troponin (hs-cTn) however its levels are chronically elevated among those with CKD and has been shown to have low specificity for Type 1 myocardial infarction hence limiting its clinical utility in the setting of suspected ACS.[16]

Aside from difficulties and ambiguities in diagnosis, CKD has been associated with poorer prognosis among patients with ACS. It has been observed that as renal function worsens, cardiovascular risk progressively increases. In fact, the prevalence of ACS among CKD patients is highest among those with ESRD on dialysis.[17] CKD has also been associated with poorer short and long term survival among patients with ACS and is associated with higher in-hospital mortality, higher incidence of major adverse cardiovascular events, higher occurrence of bleeding complications, and lower 1-year survival.[17-20] In an analysis of the Global Registry of Acute Coronary Events (GRACE) comparing ACS patients on chronic dialysis to those not on chronic dialysis, patients on chronic dialysis were more likely to present with NSTEMI and had a greater risk of in-hospital mortality, recurrent myocardial infarction, and rehospitalization.[21] The generally accepted GRACE score underestimated the risk of major events among patients on chronic dialysis.

ACS Management in CKD

Aside from the ambiguities in diagnosis and the guarded prognosis, the management of ACS in CKD is an area which is greatly equivocal. It has been shown that CKD increases the risk for both ischemic events and bleeding events.[10,22] There is a general lack of guidelines regarding the management of ACS among patients on dialysis due to the fact that most of the landmark trials in ACS excluded patients with CKD on dialysis.[12]

In the most recent guidelines of American Heart Association (AHA) and European Society of Cardiology (ESC), primary PCI for STEMI and early invasive strategy for high-risk NSTEMI is the gold standard. However, for patients previously on chronic dialysis, the data are not sufficient to recommend catheterization, and may even suggest harm.[23] However, in a retrospective analysis in Taiwan among patients with ACS and ESRD, it has been shown that PCI may have a reduced risk of mortality than those with medical treatment only.[24] Several other retrospective cohort studies among CKD patients with ACS have shown that patients who underwent CABG had better long-term survival compared to PCI.[25-27]

With regard to medical management, there is also a general lack of evidence and guidance regarding how to approach a dialysis patient with ACS. Aspirin, a recommended antiplatelet in ACS, is generally safe and tolerable among patients with ACS. Patients with ACS are also recommended to receive a second antiplatelet usually as a P2Y12 inhibitor - clopidogrel, prasugrel, or ticagrelor - however there is also a lack of evidence regarding clinical and therapeutic benefits of these agents among patients undergoing dialysis. Patients with ACS also receive an ACE-inhibitor because of its benefits in reducing MACE and improving mortality; however it is recommended to take renal dysfunction into account as a contraindication to its routine use.[28,29] Furthermore, there is less robust evidence regarding its use in dialysis patients and there is no recommended clear cut-off level of creatinine clearance that contraindicates its use.[30]

To reflect these ambiguities, it has been shown that patients with ESRD have a lower all-procedure rate (PCI, CABG, Left Heart Catheterization) compared to non-ESRD population.[31] In a report from the ACTION registry, it has been shown that among patients with NSTE-ACS, patients with CKD 4 and ESRD are more likely to be managed conservatively than undergo revascularization.[32] In another cohort study comparing treatment modalities received for ACS among ESRD and non-ESRD patients, it was found out that ESRD patients are less likely to be treated with aspirin, beta-blocker, and ACE-inhibitors compared to patients without ESRD.[33]

Risk Factors for Mortality in ACS

Despite the very complex relationship between ESRD and ACS, there is paucity of data regarding the risk factors for in-hospital morbidity and mortality specifically among dialysis patients admitted for ACS. In a cohort study done in 1998 on the US Renal Data System, predictors of mortality among dialysis patients admitted for ACS were old age (>65 years old) and presence of comorbid diabetes.[34] This was consistent with the findings in a retrospective cohort study done among an asian population on dialysis with ACS in Taiwan in 2012.[35] On the other hand, a successful angioplasty was associated with decreased risk of mortality in the Taiwanese cohort.[35] In another retrospective cohort in Pakistan, predictors of MACE and mortality among ACS patients with severe CKD undergoing PCI were cardiogenic shock, prior heart failure, or cardiac arrest possibly reflecting severity of premorbid condition rather than the severity of the ACS itself.[36]

Given the paucity of information regarding risk factors of mortality among ESRD patients with ACS, we also review other risk factors associated with mortality among patients with ACS in general. In most Asian populations, the risk factors for in-hospital mortality following ACS are age more than 65 years old, heart rate greater than 100 bpm, systolic blood pressure less than 90 to 100 mmHg, history of heart failure, reduced ejection fraction, hyperglycemia more than 180 mg/dL, and cardiac arrest on presentation.[37,38] In the ACTION Registry in the United States, similar risk factors were noted with STEMI diagnosis and previous CABG having a higher risk of in-hospital mortality.[39] Similarly, the Global Registry of Acute Coronary Events (GRACE)

Registry showed similar risk factors for in-hospital mortality but otherwise showed that patients on hemodialysis were likely to present with NSTEMI which was associated with high in-hospital mortality.[40] In a recent meta-analysis, it has also been shown that an elevated pretreatment neutrophil-lymphocyte ratio (NLR) value >5.0 predicts the risk of mortality and MACEs following ACS.[41]

METHODS

Technical and Ethical Approval

This study was technically approved by the UP-PGH Department of Medicine Research Office Technical Research Board and was approved for ethical conduct by the UP Manila Research Ethics Board (UPMREB) Panel 4.

Study Design

This is a retrospective cohort study and employed a retrospective review of electronic medical records among patients presenting with acute coronary syndrome in University of the Philippines - Philippine General Hospital (UP-PGH) from May 2021 to November 2023 on chronic hemodialysis, defined as dialysis for at least 90 days, on an outpatient basis. Although primarily an epidemiologic study which seeks to describe the population of interest, this study sought to generate associations and correlations but not establish causations between study variables for the purpose of hypothesis generation for future studies.

Study Setting and Population

The study was conducted in one site only, the University of the Philippines - Philippine General Hospital. The population was the total number of patients admitted for acute coronary syndrome in UP-PGH.

Sample Size and Sampling Method

This study employed a total enumeration sampling method. All patients with a diagnosis of acute coronary syndrome will be reviewed. From this cohort, the subpopulation with chronic kidney disease stage V on chronic hemodialysis for more than 90 days will be extracted and will be used as the final sample size for data analysis.

Eligibility Criteria

Inclusion criteria

The participant must fulfill all of the following criteria to be eligible for the study:

- Age more than or equal to 19 years old
- Filipino
- Admitted with the diagnosis of acute coronary syndrome (regardless if unstable angina, non-ST elevation MI, or ST-elevation MI) at the emergency room level diagnosed using the 4th Universal Definition of MI Expert Consensus Document by the Cardiology service
- Patients with CKD Stage V on chronic hemodialysis (defined as hemodialysis for the last 90 days[42]) or End-stage Renal Disease (ESRD) prior to the emergency room admission for acute coronary syndrome

Exclusion criteria

The participants who fulfills any of the following criteria will be ineligible for the study:

- Patients with a history of kidney transplant, CKD stage I to IV, unspecified CKD, unspecified renal failure
- Patients on peritoneal dialysis
- Patients who previously underwent kidney transplantation
- Current or past cancer diagnosis with or without chemotherapy
- Chronic (>3 months) steroid use
- Infiltrative diseases such as amyloidosis and sarcoidosis
- Diagnosed in-hospital acute coronary syndrome

Data Collection

This study is a retrospective review of electronic medical records hence all data points were extracted from the electronic record of the patients accessed through the hospital information system RADISH (Computerized Registry of Admission and Discharges) using the case number.

The charts were reviewed by the study investigators and the data points were extracted into a standardized data collection form (DCF) for encoding.

Data Encoding

The data extracted in the data collection form from the medical records was encoded by an assigned, trained, and hired research assistant into a Microsoft Excel spreadsheet. Prior to data encoding, each participant of the study was assigned a reference number to anonymize their identity. The generated data set was then counterchecked by the investigators for any errors and discrepancies, and revised accordingly. The revised data set was the one used for analysis.

Data Analysis

A statistician was hired for the analysis of the data. The collected data underwent univariate and bivariate analysis using PRISM. For the univariate analysis, the nominal data variables are presented as frequency tables and interval data variables are presented as measures of central tendency (mean with standard deviation, median, and mode).

For the bivariate analysis, the Chi-square test was utilized for nominal or dichotomous dependent variables and T-test was utilized for continuous dependent variables to obtain odds ratio. Several continuous dependent variables were also dichotomized and analyzed using Chi-square test to obtain odds ratio with p value for significance at <0.05. Multivariate analysis was not pursued due to lack of significant associations in the bivariate analysis.

RESULTS

Clinical Characteristics

A total of 48 patients were included in the final cohort of this study. The mean age of participants was 61 years old, 14 (29.2%) patients were >65 years old, and 33 (68.8%) patients were male. The most common comorbidity among participants was hypertension (91.7%) and more than half of the patients were smokers and alcoholic beverage drinkers. The rest of the comorbidities and risk factors are presented in Table 1.

Chronic Kidney Disease History

The most common cause of ESRD in this cohort is concomitant hypertensive and diabetic kidney disease (45.8%). No patient was previously scheduled for kidney transplant prior to admission. The mean duration of hemodialysis prior to admission was 31 months. In terms of dialysis access, thirty-six (75%) patients had arteriovenous fistula (AVF) as their dialysis access while the rest had a central venous catheter (either via internal jugular vein or femoral vein). Among those with an AVF, the average duration on dialysis was 35 months, while those with a central line had an average duration on dialysis of 18 months.

Clinical Status

The most common chief complaint prompting emergency room consult was chest pain (39.6%). Other chief complaints were as follows: difficulty of breathing or dyspnea (29.2%), decreased sensorium (10.4%), and abdominal pain (6.3%). The vital signs on admission summary statistics are presented in Table 2. On admission, 11 (22.9%) patients had systolic BP < 100, 18 (37.5%) patients had systolic BP >160, and 11 (22.9%) patients had heart rate >100. Seven (14.6%) patients presented with shock and dobutamine was the most common initial vasopressor or inotropic agent used on admission. Meanwhile, four (8.3%) patients presented at the emergency department in cardiac arrest.

Laboratory and Electrocardiogram Findings

The average admission laboratory tests are presented in Table 3. The average LDL-C was 74.3 mg/dL and only five (10.4%) patients had an LDL-C >55 mg/dL. Random blood sugar on admission was greater than 180 mg/dL in seven (14.6%) patients. Thirty-eight (79.2%) patients presented with anemia, 26 (54.2%) patients had a hemoglobin <100 g/dL, and 25 (52.1%) patients had a neutrophil:lymphocyte ratio of >5.

For the 12-lead electrocardiogram on admission, twenty-one (43.8%) patients had left ventricular hypertrophy, two (4.2%) had left bundle branch block, and one (2.1%) had 1st degree AV block. The most common ECG abnormality was nonspecific ST-T wave changes (64.6%).

Table 1. Comorbidities and Other Risk Factors (N=48)

	Frequency (%)
Comorbidities	
Hypertension	44 (91.7)
Heart Failure	40 (83.3)
Diabetes Mellitus	29 (60.4)
Known Cerebrovascular Disease (CVD)	16 (33.3)
Dyslipidemia / Previously on Statin Therapy	12 (25)
Previous Myocardial Infarction (MI)	12 (25)
Known Coronary Artery Disease (CAD)	12 (25)
Previous PCI / CABG	4 (8.3)
Known Peripheral Arterial Disease (PAD)	0
Other Diseases*	18 (37.5)
Other Risk Factors	
Smoker	28 (58.3)
Alcoholic drinker	28 (58.3)
Illicit drug use	5 (10.4)
Family history of ASCVD	6 (12.5)

**other diseases include lung disease, thyroid disease, liver disease*

Table 2. Vital Signs on Admission

Vital Signs	Mean (SD)	Median	Mode
Systolic BP	137 (52.50)	143	140
Diastolic BP	76 (28.83)	76	84
Heart Rate	80 (33.43)	84	84
Respiratory Rate	24 (8.83)	23	20
Temperature	36 (5.39)	36	36.5

Table 3. Laboratory Tests on Admission

	Mean (SD)
hsTrop I (ng/L)	1981 (4281)
Random blood glucose (mg/dL)	136 (78.1)
BUN (mmol/L)	20 (11.8)
Creatinine (umol/L)	872 (557)
Potassium (K) (mmol/L)	4.90 (1.23)
Calcium (Ca) (mmol/L)	2.2 (0.87)
Albumin (Alb) (g/L)	37 (5.8)
Uric Acid (mmol/L)	0.535 (1.1)
Phosphorus (Phos) (mmol/L)	2.2 (1.1)
Intact PTH (iPTH) (pg/mL)	193.8 (159.9)
Total Cholesterol (mg/dL)	119 (29)
LDL-C (mg/dL)	74.3 (54.6)
HDL-C (mg/dL)	38.1 (19)
Triglyceride (mg/dL)	151.1 (122.9)
Hemoglobin (Hgb) (g/L)	99 (21.8)
Hematocrit (Hct) %	31.1%
Neutrophil	0.77 (0.13)
Lymphocyte	0.23 (0.21)
Neutrophil:Lymphocyte Ratio	8.9 (13.6)
Platelet Count (Plt)	214 (81.7)
INR	1.25 (0.29)

Imaging Findings

All 48 patients had a chest radiograph done on admission. Two (4.2%) patients had normal findings while 34 (70.8%) patients had cardiomegaly and 25 (52.1%) patients had pulmonary congestive changes.

A total of 30 (62.5%) patients had an echocardiogram done. The most common LV geometry was normal LV geometry (33.3%) seen in ten patients while nine (30%) patients had concentric LV hypertrophy and 8 (26.7%) patients had concentric LV remodeling. The average LVEF of the entire cohort was 46%. Twelve (40%) patients had an LVEF <40% and fifteen (50%) patients had an LVEF ≥50%. Twenty-seven (90%) patients had segmental wall motion abnormalities or global hypokinesia on 2D echocardiogram.

A total of 12 (25%) patients underwent an invasive coronary angiogram. Among those who underwent coronary angiogram, the most common finding was three-vessel disease seen in six (50%) patients while four (33.3%) patients had two-vessel disease and one (8.3%) patient had one-vessel disease. Six (50%) patients had left-main involvement and three (25%) patients had chronic total occlusion of at least one vessel. The average SYNTAX score was 46 with eight (67%) having a SYNTAX score ≥ 23.

Acute Coronary Syndrome Diagnosis

Among the patient cohort, eight (17%) presented with STEMI while 40 (83%) presented NSTEMI. Among those with STEMI, six (75%) presented with Kilip II or more. While among those with NSTEMI, 17 (42.5%) had a GRACE score >140 and 27 (67.5%) had an NSTEMI TIMI risk score >2.

Medical and Invasive Management

The medical management received among the patient cohort during admission is presented in Table 4. In this patient cohort, eight (16.7%) patients had concomitant use of ACEi/ARB/ARNI and MRA during admission and upon discharge. Other cardiac medications given were digoxin (4.17%). Other commonly prescribed medications included drugs prescribed for chronic kidney disease including sevelamer, sodium bicarbonate, and EPO alfa.

Table 4. Medical Management

Medication Given during Admission	Frequency (%)	Most Common Used (%)
Aspirin	48 (100)	–
P2Y12 inhibitor	47 (97.92)	Clopidogrel (100)
Anticoagulant	47 (97.92)	Enoxaparin (100)
Statin	48 (100)	Atorvastatin (97.92)
Beta blocker	47 (97.92)	Carvedilol (76.6)
ACE inhibitor	19 (39.58)	Enalapril (100)
ARB	18 (37.5)	Telmisartan (44.4)
MRA	9 (18.75)	Spironolactone (100)
ARNI (Sacubitril + Valsartan)	10 (20.83)	–
Digoxin	2 (4.17)	–

In terms of interventions received during the same admission, one (8.3%) patient underwent percutaneous coronary intervention while no patient underwent coronary artery bypass grafting.

Clinical Outcomes

The mean length of hospital stay was 12 days. The mortality rate was 43.75% and was most commonly due to acute coronary syndrome (66.7%) and sepsis (19%). Non-cardiovascular in-hospital morbidities were hospital acquired infections (27.1%) most commonly nosocomial pneumonia, gastrointestinal bleeding (12.5%), and stroke (2.1%).

DISCUSSION

In this retrospective cohort study done over a two and a half year observational period, a total of 48 patients with ESRD were admitted at our institution for ACS - 8 with STEMI and 40 with NSTEMI. The average length of stay is 12 hospital days. This is in contrast to findings from an observational cohort done on the coronary artery disease data set of the American Heart Association, wherein the average length of hospital stay for an ACS patient with or without ESRD was 5.5 days.[42,43] Several studies have however shown that there is no difference between shorter (3-6 days) and longer (>6 day) hospital stay in terms of mortality for ACS.[44] There is a lack of data regarding the hospital length of stay specifically among ESRD patients admitted for ACS and how it correlates with short and long-term prognosis.

The most common complaint for emergency room consult was chest pain however a significant number of patients presented with dyspnea or decrease in sensorium. In a general cohort of patients with ACS, chest pain was the chief complaint in 74.8% among south asians compared to the 39.2% in our cohort.[45] Our findings were similar to a cohort of patients on dialysis admitted for ACS in the United States, wherein 44.4% presented with chest pain.[46] It is thus important to take note that in special populations, ischemic heart disease including acute myocardial infarction may manifest as anginal equivalents such as dyspnea, abdominal pain, nausea, or fatigue.

In this cohort, it can be noted that patients admitted were relatively younger at a mean age of 61 years old and only 29.2% were over 65 years old. This is in contrast to other cohorts wherein patients with severe renal impairment admitted for acute coronary syndrome had an average age of 76 years old in both a cohort from China and Denmark.[47,48]

Hypertension is the most common comorbid condition in this cohort which was present in 91.7% of patients and may possibly be due to the fact that renal parenchymal disease remains to be the leading cause of secondary hypertension. Similarly, hypertension has also been noted to be the most common comorbidity in several other cohort studies among

ACS patients on dialysis.[49] In this cohort, 37.5% of patients presented with systolic BP more than 160mmHg. On the contrary, it should also be noted that around 15% presented with shock on admission and 8.3% presented with cardiac arrest on admission. Based on an observational study in the United States, patients admitted with cardiogenic shock were 86% more likely to have CKD and 18% more likely to be on hemodialysis.[49] Based on these, it can be surmised that a patient with ESRD is considered at risk of both spectrums either presenting as severe hypertension or hypotension and shock. Furthermore, based on an analysis of the ACS-QUIK cohort, the relationship between admitting SBP and MACE had a U-shape curve with inflection points at SBP <100 mmHg and SBP >159mmHg, indicating high risk for cardiovascular events if the admitting SBP was beyond the 100-159 mmHg range.[50] However, there was no significant association between SBP < 100 mmHg and SBP >160 mmHg with mortality in this cohort.

The second most common comorbid condition was heart failure and this may pose significant struggles in its management mainly because several medications which have shown to reduce cardiovascular events in HF, specifically HFrEF, may be more difficult to initiate, sustain, and adjust in ESRD. Firstly, SGLT2 inhibitors, the only medication which has Class I level of recommendation across the whole HF spectrum, are contraindicated among those with eGFR <20-25 mg/dL mainly because the major heart failure trials excluded patients with an eGFR below this threshold. Furthermore, the combination of ACEi/ARNI/ARB with an MRA also poses higher risks for hyperkalemia which also limits its concomitant use in ESRD.[51] To highlight this in this cohort, only 8 (16.7%) patients had concomitant use of ACEi/ARB/ARNI and MRA despite the mean potassium being within normal limits at 4.9 mmol/L.

In terms of atherogenesis and LDL-C levels, it is interesting to note that only 5 (10.4%) patients presented with LDL-C more than 55 mg/dL on admission. To review the latest ESC guidelines on acute coronary syndrome and dyslipidemia, an LDL-C < 55 mg/dL is the target for patients with clinical ASCVD including acute coronary syndrome in order to prevent further cardiovascular events.[52,53] Despite the majority of patients in our cohort being on target in terms of LDL-C, the patients still presented with acute coronary syndrome and may support that other pathologic mechanisms of atherosclerosis exist in ESRD beyond simple hyperlipidemia such as inflammation and endothelial dysfunction.[9-11] Moreover, one of the established risk factors for accelerated atherosclerosis in CKD is hyper-phosphatemia.[54] In our cohort, it was noted that the average phosphorus level was beyond the normal range indicating that this risk factor was indeed present in our cohort and should be considered as a therapeutic target.

Anemia and inflammation also plays an important role in acute coronary syndrome as it has been shown to be associated with an increased mortality.[55,56] In this cohort, 79.2% of patients presented with anemia with 54.2% of patients having hemoglobin <100 g/dL. The neutrophil:lymphocyte ratio has been used as a laboratory index to quantify ongoing inflammation and a ratio more than 5 has been associated with poorer prognosis in previous observational studies among patients with ACS. In this cohort, 25 (52.1%) patients had a neutrophil:lymphocyte ratio of >5. However, both anemia and NLR showed no significant associations with mortality in this cohort.

In terms of the electrocardiogram (ECG) and chest radiograph findings, 43.8% had left ventricular hypertrophy (LVH) by Sokolow-Lyon or Cornell criteria on ECG and 70.8% had cardiomegaly on chest radiography which may signify these as the sequelae of chronic hypertension. It is established that in ESRD patients, LVH detected by ECG is the most common manifestation of cardiovascular disease and strongly predicts cardiovascular morbidity and mortality.[57] Likewise, cardiomegaly by radiograph is associated with cardiovascular mortality and all-cause mortality.[58.59]

Despite these findings, the most common LV geometry noted on the two-dimensional echocardiogram was normal LV geometry. Despite noting that 50% of patients presented with an left ventricular ejection fraction (LVEF) ≥50%, the average LVEF was 46% and nearly 90% of patients presented with segmental wall motion abnormalities indicative of the high propensity for coronary artery disease in this cohort. In the Strong Heart study, the presence of echocardiographic wall motion abnormalities was associated with a 2.4-3.4 fold higher risk of cardiovascular morbidity and mortality.[60] In addition, a lower LVEF is associated with high mortality among ESRD patients with coronary artery disease.[61] Hence the presence of these wall motion abnormalities and below normal LVEF in our cohort is indicative of poorer prognosis.

Among those who underwent coronary angiogram, the most common findings was three-vessel coronary artery disease which was present in 50% in this cohort. This was similar to the findings in a cohort study in Korea which showed that three-vessel coronary artery disease was the most common angiographic finding among CKD Stage V patients at 36.5%.[62] Most of the patients in this cohort had complex coronary anatomy based on the SYNTAX score and this may be due to the intricate interplay of vascular calcification on top of the usual risk factors for coronary artery disease present in the CKD population.[57] To further support this, a prospective cohort study among CKD patients undergoing angiogram showed that as CKD stage progresses, the complexity of coronary lesions worsens.[63]

In terms of outcomes, we found out that several parameters were present in this cohort which are suggestive of a worse prognosis. In terms of established prognostication scores, a higher proportion of patients presented with Killip II or more for STEMI and TIMI score >2 for NSTEMI in our study cohort. However, more patients in our cohort presented with a GRACE score <140, the supposed cut off for a higher risk ACS based on the GRACE registry. However, based

on an analysis of the GRACE registry, the GRACE score underestimated mortality and morbidity events in its dialytic cohort and may reflect this similar finding in our cohort. To highlight our cohort's worse prognosis even further, the mortality rate in this cohort was high at 43.75% with acute coronary syndrome being the most common cause of death. This is in contrast to a cohort of mixed CKD and non-CKD patients where in-hospital mortality was 9.6% for STEMI and 13% for NSTEMI.[64] In a cohort study among patients with moderate or severe renal impairment (eGFR <60mL/min) admitted for ACS, in-hospital mortality rate was 18%.[48]

Aside from a high in-hospital mortality rate in our study cohort, it should be noted that the rate of in-hospital morbidities were also high. The in-hospital gastrointestinal bleeding rate in our cohort was 12.5% compared to the 1.3 to 8.9% reported in a study among ACS patients without CKD.[65] Among patients with ACS, gastrointestinal bleeding is identified as an independent predictor of mortality and worse clinical outcomes in the said study. In the TRANSLATE-ACS cohort study which compared bleeding rates of ACS patients across different CKD stages, those with CKD stage IV and V were at a significantly higher risk of bleeding compared to CKD stages I-III.[66] Our study however did not show a correlation between in-hospital GI bleeding and mortality.

In terms of medical management, the cornerstone of ACS treatment remains to be dual antiplatelet therapy, high intensity statin, beta blocker, and ACE inhibitor.[52] In this cohort, there was a high propensity of prescribing dual antiplatelet (97.92%), high intensity statin (100%), and beta blocker (97.92%). However, only 39.58% were prescribed with an ACE inhibitor while 37.5% were prescribed an ARB. In this cohort, there was no significant difference in mortality between groups given ACEi and ARBs.

Indeed, the low sample size is acknowledged by the investigators as the major limitation of this study but the findings can still serve as hypothesis generating for future studies. Other limitations of this study include the lack of certain diagnostics for all patients including two-dimensional echocardiography and invasive coronary angiogram.

CONCLUSION

This retrospective study presents the clinical profile and outcomes of patients with end-stage renal disease presenting with acute coronary syndrome in a tertiary government hospital in the Philippines. This study the high mortality rate among patients with ESRD presenting with ACS. Our study portrays that patients with ESRD present with higher risk features as evidenced by extremes of blood pressure on admission, clinically significant laboratory abnormalities and derangements, adverse electrocardiographic, radiographic, echocardiographic, and angiographic findings, higher risk stratification based on risk prognostication scores, and high in-hospital morbidity especially gastrointestinal bleeding.

Hence for a more comprehensive description of the cohort, we recommend that future studies have a larger sample size and that comparisons with a non-dialytic and non-CKD cohort be pursued.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

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