Development of a Risk Prediction Score for Acute Kidney Injury in Critically-ill Septic Filipino Patients Admitted in Perpetual Succour Hospital

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Abstract

Introduction: Acute kidney injury (AKI) is a lethal complication of critical illness characterized by the rapid loss of the kidney's excretory function encountered in 50% of intensive care unit (ICU) admissions. Its impact on the outcome of critically ill patients makes AKI a significant cause of morbidity and mortality.

Objectives: To develop and validate an acute kidney injury risk prediction score based on routinely available variables and common laboratories of admitted critically-ill septic Filipino patients.

Methods: This is a prospective cohort study conducted in a tertiary hospital in Cebu from February to September 2020. The data of 2545 patients were identified by chart review but only 607 patients with a quick Sepsis Organ Failure Assessment Score (qSOFA) score of ≥2 were included in the pre-screening. After stratified sampling, a total of 198 septic ICU patients were enrolled. Demographic profile, laboratory results and outcome data were collated. Variables were screened then stepwise forward elimination was done to identify the significant predictors. An AKI risk score model was developed with binomial regression analysis by identifying independent prognostic factors. The diagnostic ability of the model was determined by the Area under the Receiver Operating Characteristics (AuROC).

Results: AKI developed in 155 (78%) patients. The significant predictors for Acute Kidney Injury were age, hypertension, atherosclerotic cardiovascular disease, weight, white blood count, creatinine, and BUN. An AKI prediction model with a cut off score of 161.9 was made with a fair diagnostic ability for predicting AKI at 0.79 based on AuROC.

Conclusion: The developed risk prediction tool using routinely available variables is found to be fairly accurate to predict the development of AKI among critically ill septic patients.

Keywords: Acute kidney injury, Risk prediction score, Critically-ill patients, sepsis

Introduction

Despite its seemingly recent emergence in the annals of medicine, acute kidney injury (AKI), as an ailment, has long afflicted humanity. Its historical roots are presumed to predate science but its murky history was only unveiled in the era of pastoral medicine; first, when Galen identified suppressed urine output as a differential diagnosis for a distended bladder, and later on, in the 18th century, when Giovanni Batista Morgagni sorted suppressed urine (formerly known as *ischuria*) into different organ-based classifications.[1] As modern science developed, so did our understanding of AKI, its epidemiology and its clinical course.

At present, AKI remains one of the most challenging and debilitating complications of critical illness. With an annual worldwide incidence of 13 million cases and an estimated 2 million fatalities, it is a significant cause of in-hospital admissions and mortalities with high financial burden.[2] In the Philippines, the 2018 data from the World Health Organization ranked kidney disease as the 7th cause of death in the country with 21,894 deaths or 3.59% of all mortalities.[3]

Sepsis is the most common cause of AKI in the critically ill. In a study by Peerapornratana S. et al, sepsis is found in about 40-50% of patients with AKI in the ICU.[4] Despite this, the mechanisms of sepsis in inducing AKI is still not well understood. The preponderant theory attributes

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sepsis-associated AKI to the decrease in renal perfusion and eventual renal tubular cell death.[5]

Nevertheless, despite its prevalence, early diagnosis of AKI continues to be a daunting task for any clinician. Thus, early identification of AKI among the high-risk population could not only provide strategies for prevention but is also potentially life-saving. Over the past several years, several risk stratification tools to predict AKI in specialized settings (e.g. after general or cardiac surgery) have been developed; however, only a few models catered to septic patients in the medical ICU.[6] The researchers believe that there is a need to develop improved clinical risk prediction tools for AKI in critically ill septic patients to provide clinicians information for prevention, early diagnosis, and targeted interventions. The development of a risk stratification score based on routinely available clinical variables would accurately predict the risk for AKI in critically ill septic patients and could potentially improve the management.

AKI is a life-threatening complication of critical illness associated with significant morbidity and mortality. It is an independent risk factor for death and survivors are at a higher risk of developing chronic kidney disease.[2] Understandably, attempts to recognize AKI early are made to provide opportunities for preventive and therapeutic mediations. Over the past several years, several risk scoring tools have been developed to predict AKI development and contributed to a more enhanced comprehension of the course of AKI.

Fletchet, et al developed an online risk scoring model for AKI prediction using common clinical variables and compared its predictive ability against neutrophil gelatinase-associated lipocalin (NGAL), a novel biomarker for kidney injury.[9] In this multicenter prospective cohort study, a total of 4640 adult patients in multidisciplinary ICUs were enrolled and creation of the model was based on NGAL measurement taken on the day of hospitalization and clinical data taken before, during and a day after ICU admission. This study concluded that AKI developed within the first seven days of admission and NGAL does not add value to the predictive performance of the model, both when used as a sole predictor or in combination with clinical data.

Another risk stratification tool to predict AKI was developed by Malhora, et al using only common clinical variables.[10] In this multicenter prospective study, a total of 717 medical ICU patients from the University of California San Diego and 1300 patients from the medical-surgical ICU of Mayo Clinic in the United States were enrolled and screened for predictor variables for AKI within 48hours of ICU admission. The primary outcome was the development of AKI within seven days. In this study, 37.2% of patients developed AKI and cited chronic kidney disease, chronic liver disease, congestive heart failure, hypertension, atherosclerotic coronary disease, acidosis, nephrotoxin exposure, sepsis, mechanical ventilation, and anemia as the independent predictors of AKI. The developed tool showed good calibration and achieved a fair diagnostic ability of 0.79 by Area under the Receiving Operating Characteristic (AuROC). This model is simple, reliable, and only used readily available clinical variables that can be used to predict AKI at ICU admission.

Significance of the Study. Despite the availability of several AKI predictive models, most of the existing tools cater to specific critical care settings such as AKI after general or cardiac surgery. Interestingly, regardless of the strong association between sepsis and kidney failure, there are only a few risk stratification tools that investigates the septic and critically ill population. Furthermore, some of these risk stratification tools make use of novel biomarkers such as NGAL and CyC that are not only costly but are scarcely available and may be clinically heterogeneous making them volatile sole predictors of AKI.

Although there are other validated models that utilize routinely available variables, the number of factors needed for computation range between 10-20 and require repeat entries for different hospitalization days making them cumbersome to use. With these things in consideration, the researchers of this study hope to develop a risk stratification tool that will hopefully add to the scant number of predictive AKI tools that serve the septic patients in the medical ICU. By making a model that can be readily used in the emergency department on the day of admission using fewer common clinical variables but still possess fair accuracy, the authors aim to help clinicians identify critically ill patients at risk to develop AKI.

Research Question. Can a risk stratification score based on the demographic profile, co-morbidities and routine clinical variables predict the risk to develop Acute kidney injury in critically-ill septic Filipino patients admitted in a tertiary hospital?

General Objectives. To develop and validate an acute kidney injury risk prediction score based on routinely available variables such as the demographic profile, chronic co-morbidities and common laboratories of critically-ill septic Filipino patients admitted in a tertiary hospital.

Specific Objectives.

1. To determine the demographic profile of patients admitted as critically ill septic patients as to: age, sex, location of residence, chief complaints, and cause of sepsis
2. To determine the clinical characteristics of critically-ill septic patients as to: illness day, vital signs, weight, urine output, and quick Sepsis Organ Failure Assessment (qSOFA) score
3. To determine the laboratory findings of critically-ill septic patients as to: complete blood count (CBC), absolute neutrophil count, arterial blood gas (ABG), creatinine, mean estimated glomerular filtration rate (eGFR), blood urea nitrogen (BUN) level, and BUN-Creatinine ratio

Table I. Demographic Profile of Patients Admitted as Critically Ill and Septic

Age (in years)	f	%	p-value
19-30	24	12%	0.01*
31-40	9	5%	0.351
41-50	11	6%	0.365
51-60	44	22%	0.390
61-70	47	24%	0.322
>70	60	30%	
Sex	20	10	
Male	97	49%	0.68
Female	101	51%	
Location			
Cebu City	129	65%	0.23
Cebu Province	39	20%	
Lapu-lapu	7	4%	
Leyte	1	1%	
Mandaue	22	11%	

Table II. Common Complaints of the Patients

Chief Complaints	f	%	p- value
Abdominal Pain	4	2%	0.712
Abdominal Pain, Fever Anorexia	1	1%	
Anorexia	1	1%	
Body Malaise	9	5%	
Change In Sensorium	1	1%	
Confusion	1	1%	
Constipation	1	1%	
Cough	6	3%	
Cough And Fever	7	4%	
Cough, Dyspnea	3	2%	
Cough, Fever, Shortness Of Breath	1	1%	
Cough, Fever,Dyspnea	4	2%	
Decrease In Sensorium	4	2%	
Dyspnea	100	51%	
Epigastric Pain	1	1%	
Exertional Dyspnea	2	1%	
Fever	19	10%	
Fever And Dyspnea	4	2%	
Fever And LBM	1	1%	
Fever, Productive Cough	1	1%	
Hematemesis	2	1%	
Hematemesis, Melena	1	1%	
Hematuria	1	1%	
LBM	2	1%	
Loss Of Consciousness	5	3%	
Melena	1	1%	
Non Healing Wound	2	1%	
Oliguria	1	1%	
Palpitations	1	1%	
Right Sided Weakness	3	2%	
Swelling Right Leg	1	1%	
Unresponsiveness	3	2%	
Vaginal Spotting, Dyspnea	1	1%	
Vomiting	1	1%	

*Factor is Significant at 0.05 using Binary Logistic Regression

4. To determine the proportion of patients who developed kidney failure
5. To determine the proportion of patients who had subsequent renal replacement therapy (hemodialysis)
6. To determine the optimal AKI risk prediction cut-off score which would generate a clinically acceptable accuracy that could predict acute kidney injury in critically ill septic patients
7. To determine the patients' hospital outcome: Recovered, Expired, Transferred, or discharged against medical advice (DAMA)

Scope and Limitations. This is a single center study that aims to develop an AKI risk predictive model from common clinical variables of septic patients in the medical ICU. Electronic medical records of 1,234 patients admitted between February to September 2020 were reviewed but only 198 septic patients with a quick Sepsis Organ Failure Assessment (qSOFA) score of ≥ 2 were included in the study after screening and stratified sampling. Data were collected following defined risk variables to develop and validate the study cohorts. Easily available parameters and simple categorical formulation were utilized to estimate AKI risk.

However, the researchers also acknowledge that despite the heterogeneous population, the small sample size is a major limitation of this study since this may not be representative of other patient groups. Additionally, some variables such as important laboratory tests were not uniformly ordered or present due to extraneous factors such as financial constraints, physician preference and prioritization of labs, and for some, untimely death. Also, an accurate medical history cannot be ascertained since a portion of the patients were comatose or unconscious on admission, while others have no accompanying family members who are knowledgeable of their medical information. Lastly, some patients enrolled in this study developed AKI on the second day of admission thus restricting the usefulness of this study for a broader population.

Methods

Study Design and Setting. This is an analytical retrospective study conducted at Perpetual Succour Hospital, Gorordo Avenue, Cebu City covering a period of six months, from February 1 to September 30, 2020.

Study Population. From an initial 2,545 patients admitted in a tertiary hospital between February to September 2020, only 607 patients with a quick Sepsis Organ Failure Assessment Score (qSOFA) score of ≥ 2 were included in the pre-screening. Stratified random sampling using the month of admission as a stratum was then employed to come up with a total of 198 septic ICU patients included in the model development.

Inclusion Criteria. The study included all Filipino patients admitted in Perpetual Succour Hospital who are at least 18 years old and is diagnosed with sepsis with a qSOFA score of ≥ 2.

Exclusion Criteria. The study did not include patients who have: Advanced (Stage 5) chronic kidney disease

Table III. The Major Causes of Sepsis of Patients

Cause of Sepsis	f	%	p-value
Ascending Cholangitis	1	1%	0.321
Aspiration Pneumonia	1	1%	
Aspiration Pneumonia	2	1%	
Aspiration Pneumonia, Urosepsis	2	1%	
Bacterial Peritonitis	2	1%	
Breast Abscess	1	1%	
Cellulitis	9	5%	
Cellulitis, Urosepsis, Community Acquired Pneumonia	2	1%	
Community Acquired Pneumonia	41	21%	
Community Acquired Pneumonia, Cellulitis	1	1%	
Community Acquired Pneumonia,Urosepsis	1	1%	
Covid 19 Pneumonia	71	36%	
Covid 19 Pneumonia, Infected Ulcer	1	1%	
Covid19 Infection	6	3%	
Diabetic Foot Gangrene	1	1%	
Empyema Thoracis	2	1%	
Gangrenous Sigmoid Colon With Volvulus	1	1%	
Gram Negative Bacteremia	3	2%	
Gram Positive Bacteremia	1	1%	
Gram Positive Bacteremia And Urinary Tract Infection	1	1%	
Hospital Acquired Pneumonia	10	5%	
Infected Wound	4	2%	
Infectious Diarrhea	1	1%	
Infectious Diarrhea	1	1%	
Infectious Diarrhea, Community Acquired Pnuemonia	1	1%	
Intestinal Amoebiases	1	1%	
Klebsiela Bacteremia	1	1%	
Nonhealing Wound	1	1%	
Pelvic Infection	1	1%	
Pneumonia In An Immunocompromised Host	2	1%	
Sepsis Sec. To Cellulitis, Left Leg	1	1%	
Urinart Tract Infection	1	1%	
Urinary Tract Infection	1	1%	
Urosepsis	13	7%	
Urosepsis, Aspiration Pneumonia	1	1%	
Urosepsis, Community Acquired Pneumonia	2	1%	
Urosepsis, Ruptured Appendicitis	2	1%	
Urosepsis. Community Acquired Pneumonia	2	1%	
Ventilator Associated Pneumonia	2	1%	

*Factor is Significant at 0.05 using Binary Logistic Regression

(CKD), anuria, urine output < 30 ml within 24 hours from admission, and diagnosed with AKI according to the Kidney Disease: Improving Global Outcomes (KDIGO) serum creatinine criteria at the time of screening.

Data Collection. After obtaining approval from the Institutional Ethics and Review Board (IERB), hospital administrator and the department chair of Internal Medicine to conduct the study, the charts of 2,545 admitted patients were reviewed. In a pre-screening

Table IV. Patient Comorbidities

Comorbidity	f	%	p-value
Diabetes	43	22	0.061
Hypertension	77	39	0.010*
Chronic Kidney Disease	39	20	0.001*
Atherosclerotic Coronary Vessel Disease	13	7	0.001*
Bronchial Asthma	2	1	0.351
COPD	1	0	0.365
Malignancy	3	1	0.390
Hematologic Illness	0	0	0.322
Rheumatologic Illness	0	0	0.428
No comorbid illness	20	10	0.122

*Factor is Significant at 0.05 using Binary Logistic Regression

Table V. Characteristics of Patients with AKI

Clinical Presentation	Mean	SD	p-value
Illness Day	6.84	13.50	0.86
Temperature (°C)	36.99	0.90	0.08
Systolic Blood Pressure (mmHg)	109.82	36.09	0.39
Diastolic Blood Pressure (mmHg)	67.03	22.12	0.98
Mean Arterial Pressure (mmHg)	81.41	26.07	0.88
Heart Rate (bpm)	102.79	26.07	0.88
Respiratory rate (cpm)	28.96	9.41	0.59
Oxygen saturation (%)	78.58	29.10	0.002*
Estimated weight (kg)	65.20	10.78	0.002*
Urine output (cc/kg/hr)	0.72	0.60	0.000*
qSOFA score	2.23	0.45	0.23

*Factor is Significant at 0.05 using Binary Logistic Regression
Abbreviations: qSOFA = quick Sepsis Organ Failure Assessment

Table VI. Diagnostic Results of the Patients

Diagnostic Tests	Mean	SD	p-value
WBC (µL)	15.21	9.52	0.036*
Neutrophils (%)	82.40	13.91	0.49
Lymphocytes (%)	10.00	11.00	0.47
Neutrophil bands (%)	0.04	0.24	0.71
Absolute Neutrophil Count (/mm^3)	1873.57	2760.28	0.74
Hemoglobin (g/dL)	11.90	2.79	0.43
Hematocrit (%)	36.20	9.74	0.49
Platelet (µL)	209.70	113.51	0.55
pH	6.81	1.91	0.94
pCO_2 (mmHg)	28.31	12.76	0.43
HCO_3 (meq/L)	13.91	6.30	0.61
Oxygen saturation (%)	82.87	25.08	0.13
PaO_2 (mmHg)	85.57	65.50	0.08
FiO_2 (%)	42.45	39.69	0.17
P/F Ratio (mmHg)	250.87	185.59	0.37
Admitting creatinine (mg/dL)	2.62	2.92	0.001*
eGFR (mL/min/1.73m^2)	52.19	50.04	0.000*
BUN (mg/dL)	24.08	36.32	0.021*
BUN/Creatinine Ratio	14.41	12.48	0.17

*Factor is Significant at 0.05 using Binary Logistic Regression
Abbreviations: WBC = white blood count, pH = power of hydrogen, PCO2 = partial pressure of carbon dioxide, HCO3 = bicarbonate, paO2 = partial pressure of oxygen, FiO2 = fraction of inspired oxygen, P/F ratio = PaO2/FiO2 ratio, eGFR = estimated glomerular filtration rate, BUN = blood urea nitrogen

Table VII. Cross-tabulation of Patients Who Developed Kidney Injury and Had Subsequent Hemodialysis

Hemodialysis Status	AKI		
	No	Yes	Total
No	43 (22%)	113 (57%)	156 (79%)
Yes	0	42 (21%)	42 (21%))
Total	43 (22%)	155 (78%)	198 (100%)

Table VIII. Summary of Significant Variables for Predictive Model Use

Diagnostic Tests	p-value
Age	0.000
Chronic Kidney Disease	0.001
Hypertension	0.010
Atherosclerotic Coronary Vessel Disease	0.001
Admitting Creatinine	0.001
eGFR	0.000
BUN	0.021
Oygen saturation	0.054
Estimated weight	0.000
Urine output	0.000
WBC	0.176

step, only 607 patients with a qSOFA score of ≥2 were included for stratified random sampling. A final total of 198 patients were then included in the model development. Patient's data such as demographic profile, clinical findings, laboratory results and hospital outcomes were gathered and tabulated in the data collection form and followed throughout their admission

Statistical Analysis. Continuous variables were expressed as the mean (±SD) or median and interquartile range and analyzed by *unpaired t-test* or the *Wilcoxon rank-sum test*, as appropriate. Categorical variables are expressed as absolute (n) and relative (%) frequency. In a preprocessing step, significant variables were identified and analyzed by *chi-square test* or *Fisher's exact test*, as appropriate.

To determine which variables will be included in the predictive model, stepwise forward elimination using binary logistic regression to calculate for the odds ratio of the significant variables was applied. Component variables were multiplied together then converted these factors into additive risk points to come up with a cut-off score to predict AKI. Cut-off scores were determined where the coordinates registered approximately 0.80 in terms of specificity and sensitivity. Subsequently, the Area under the Receiver Operating Characteristics (AuROC) was used to measure the accuracy level of the model (AKI Risk Index).

Ethical Considerations. All patients were designated according to numbers instead of their names. Patients' data were collated with utmost confidentiality.

This paper was not supported by any company or individual who will benefit financially from the results of the study whether directly or indirectly. The researchers hereby declare no conflict of interest as they wrote this paper. They did not receive any financial assistance from a company or individual believed to benefit from this study.

Results

Patients included in our study were mostly elderly females (51%), aged 70 years old and above (*Table I*). Majority of these patients were residents of Cebu City at the time of admission. Age significantly predicted the likelihood of AKI (*p=0.01*) while sex and location showed no significant effect to the occurrence of AKI (*p>0.05*)

Table II shows that dyspnea was the most frequent complaint on admission amounting to 51%, followed by fever (10%), body malaise (5%), cough and fever (4%), and loss of consciousness (3%). The chief complaints, however, did not significantly correlate to the likelihood of having AKI.

Majority of the etiology of sepsis was attributed to Coronavirus Disease-19 (COVID-19) pneumonia with 36%, followed by Community Acquired Pneumonia with 21%, then Urosepsis with 7% and Cellulitis with 5%. Nevertheless, the different causes of sepsis did not provide sufficient evidence to explain AKI (*p>0.05*).

Hypertension is the most common co-morbid illness among the admitted critically ill COVID-19 patients with

Table IX. The AKI Risk Predictors Based on the Binomial Logistic Regression for the Development of the AKI Predictive Model: Step 1

Predictor	B	S.E.	Wald	df	p-value	Odds Ratio
Age	0.05	0.01	25.71	1.00	0.00	1.06
Chronic Kidney DIsease	3.39	1.03	10.96	1.00	0.00	0.03
Hypertension	0.65	0.25	6.66	1.00	0.01	1.91
Atherosclerotic Coronary Vessel Disease	0.64	0.20	10.25	1.00	0.00	1.89
Admitting creatinine	0.67	0.20	10.60	1.00	0.00	1.94
eGFR	0.03	0.01	23.93	1.00	0.02	0.91
BUN	0.03	0.01	5.36	1.00	0.02	1.03
Oxygen saturation	0.02	0.01	3.72	1.00	0.05	0.98
Estimated weight	0.06	0.02	13.25	1.00	0.00	1.06
Urine Output	2.30	0.41	31.08	1.00	0.00	0.10
WBC	0.03	0.02	1.83	1.00	0.18	1.03

*Factor is Significant at 0.05 using Binary Logistic Regression

Table X. The AKI Risk Predictors Based on the Binomial Logistic Regression for the Development of the AKI Predictive Model: Step 2

Predictor	B	Std Error	Wald	df	p-value	Odds Ratio
Age	0.05	0.01	25.71	1.00	0.00	1.06
Hypertension	0.65	0.25	6.66	1.00	0.01	1.91
Atherosclerotic Coronary Vessel Disease	0.64	0.20	10.25	1.00	0.00	1.89
Admitting creatinine	0.67	0.20	10.60	1.00	0.00	1.94
BUN	0.03	0.01	5.36	1.00	0.02	1.03
Estimated weight	0.06	0.02	13.25	1.00	0.00	1.06
WBC	0.03	0.02	1.83	1.00	0.18	1.03

*Factor is Significant at 0.05 using Binary Logistic Regression

39%, followed by Diabetes at 22% and chronic kidney disease at 20%. Incidentally, hypertension, along with chronic kidney disease and atherosclerotic vessel disease, were also statistically good predictors of AKI.

Table V shows that parameters such as oxygen saturation, estimated weight, and urine output predicted AKI significantly ($p<0.005$). However, other clinical presentations were not statistically significant.

In the same table, WBC, admitting creatinine, BUN, and eGFR were statistically significant ($p<0.05$) making them good indices for the AKI predictive model development.

A total of 155 out of 198 patients (78%) developed AKI with 42 patients (21%) eventually needing hemodialysis.

Table VIII summarizes the different parameters that demonstrated statistical significance ($p<0.05$) making them candidates for use in the AKI predictive tool.

After the identification of the statistically significant variables, a binomial logistic regression was done to facilitate the measurement of the odds ratio (OR) of these variables (*Table IX*). An OR > 1 means that the likelihood of getting AKI is increased in these variables.

Table XI. The AKI Predictive Model Based on Risk Predictors: Step 3

Age*1.055 + Admitting Creatinine*1.944 + BUN*1.028 + Hypertension*1.907 + Atherosclerotic coronary vessel disease*1.889 + WBC*1.030 + Estimated Weight*1.064

Table XII. Determination of the Diagnostic Ability of the Risk Model for AKI Risk Prediction (AUC)

Test Result Variable(s)				
Area	Std. Error	Asymptotic Sig.	Asymptotic 95% CI	
			Lower Bound	Upper Bound
0.792	0.040	0.000	0.643	0.801

Table XIII. Determination of the Diagnostic Ability of the Risk Model for Prediction of the Risk for Hemodialysis Initiation (AUC)

Test Result Variable(s):				
Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% CI	
			Lower Bound	Upper Bound
0.523	0.058	0.705	0.409	0.637

Only variables with an OR > 1 were included in the final predictive model.

Table X shows the stepwise forward elimination of insignificant parameters and retention of the identified significant variables. These variables were included in the AKI predictive model as potential AKI indices. It is noted that the admitting creatinine contributes most to the likelihood of getting AKI, followed by the presence of hypertension and atherosclerotic coronary vessel disease.

Stepwise forward elimination regression analysis shown in *Tables IX* and *X* can be described with the equation shown in *Table XI*.

The diagnostic ability of the risk model was determined by the area under the receiver operating characteristic curve (AuROC). AuROC values and their corresponding diagnostic strength equivalents are the following[11]:

- 0.90-1.00: excellent accuracy,
- 0.80-0.89: good accuracy,
- 0.70-0.79: fair accuracy,
- 0.60-0.69: poor accuracy,
- 0.50: no discriminating ability.

Table XII shows that the AuROC value for this model is at 0.792 which means that the model used has a 79% accuracy of classifying correctly those who had AKI and

Table XIV. The AKI Risk Predictors Based on the Binomial Logistic Regression for the Development of the AKI Predictive Model: Step 4

Predictors	OR	Conditions for the Model
Age	1.055	If ≥54 = score 1.055, else 0
Hypertension	1.907	If yes, = score 1.907, else 0
Atherosclerotic Coronary Vessel Disease	1.889	If yes = score 1.889, else 0
Admitting creatinine	1.944	If ≥1.07 = score 1.944, else 0
BUN	1.028	If ≥19.5 = score 1.028, else 0
Estimated weight	1.064	If ≥59 = score 1.064, else 0
WBC	1.030	If ≥7.56 = score 1.030, else 0
Total Score	**1.321**	**If ≥161.9 = score as AKI**

*Cutoff Scores were based on the ROC Coordinates of the Curve with ≈ 0.80

Table XV. The Distribution of Patient Outcomes

Predictors	f	%
Recovered	89	45%
Died	106	54%
Transferred	0	0%
Discharged Against Medical Advice (DAMA)	3	2%

at the same time excluding correctly those who did not manifest the condition.

Table XIII shows that the developed risk model only recorded an AuROC of 0.52 or 52% accuracy in predicting the risk for hemodialysis initiation. This means that the aggregated factors included in the index has no discriminating ability to predict the need to start hemodialysis.

The cut-off total score of 161.9 was used in the formulation of AKI detection as dictated by the receiving operating characteristic (ROC) based on the coordinates at ≈ 0.80 (*sensitivity/specificity*).

Table XV revealed that majority of the patients in this study died (54%) while 45% recovered. A small minority of patients (2%) went home against medical advice.

Discussion

Majority of the patients in this study belonged to the older population, of which almost a third (30%) were more than 70 years old. It was illustrated that age significantly predicted the likelihood of developing AKI which is comparable to multiple studies reporting advanced age as a predisposition to having renal injury.[12] According to Kane-Gil et al, age is one factor that determines the risk for AKI due to the elderly's decreased renal reserve and altered kidney function inhibiting renal recovery following injury.[13] A similar study by Ishani, A. et al and Hutchens MP et al reported that older critically ill patients 75 years old and above have a 20% greater rate of AKI compared to younger patients (18-54 years old).[12,14].

On the other hand, females comprised the larger proportion of patients in this study (>51%) which is contrary to the established prevalence in the world and in the Philippines where males are noted to be the more commonly affected gender with 51-60% of reported cases compared to females.[15] Additionally, gender did not show association with AKI prediction in this research contrasting what is cited in literature that reported the correlation of male sex with increased incidence of hospital-associated AKI. As reported by Fisher M. et al men above 50 years old are not only associated with increased AKI but also a higher mortality risk.[16]

The symptomatology of acute kidney injury largely depends on the etiology and severity of renal injury. Sepsis is a well-established cause of AKI accounting for 30 to as high as 50% of all cases in the critical care setting. The hypoperfusion of kidneys due to sepsis-induced arterial vasodilation is a principal hallmark of sepsis-associated AKI.[5] Although most patients with mild to moderate AKI exhibit mild to no symptoms, those who presented with severe cases, usually reported manifestations ranging from fatigue, oliguria, nausea, vomiting to dyspnea and confusion.[17] In this study, dyspnea was the most frequent complaint on admission with 51%, followed by fever, body malaise, cough and fatigue. Coincidentally, the most common cause of sepsis in patients who developed AKI in this study was COVID-19 pneumonia with 36%. This finding could be explained by the fact that, at the time, it was the surge of the COVID-19 pandemic in the locality. Nevertheless, respiratory illness as a major cause of sepsis that developed renal injury is commonplace. Liu et al showed in a study that pulmonary infections on top of abdominal infections were the most common source of infection in patients with sepsis who developed AKI.[18] However, in the study, symptomatology and the cause of sepsis showed no significant relationship to AKI development.

In terms of clinical presentation, oxygen saturation, weight and urine output predicted AKI significantly. Panitchote, A. et al, cited hypoxemia, along with systemic acidosis, as an important contributor to renal damage due to the tendency to affect renal perfusion in virtue of the gas exchange abnormalities.[19] Alternatively, Macedo (2015) emphasized the importance of urine volume of <0.5 ml/kg/hr for six hours as an early predictor of AKI while Sunmi Ju et al highlighted the close association between high BMI and risk of AKI development due to the hemodynamic changes in the glomerulus brought about by obesity.[20,21]

The SOFA score, on the other hand, did not show statistical significance to be considered a good determinant for AKI prediction. This contrasts with existing literature that highlights the prognostic value of SOFA score in predicting septic AKI and in-hospital mortality. In a study by Chao-Wei Lee et al on 33 septic surgical ICU patients, 81% of patients who were diagnosed with sepsis had high SOFA scores on admission and had varying degrees of AKI.[22] It concluded that the admitting SOFA score demonstrated high sensitivity, specificity, and prognostic value for septic AKI.

As for diagnostic tests, our study demonstrated that WBC count, with a *p=0.036*, is a good predictor of AKI. Fangfang F. et al determined whether WBC count predicts the odds of kidney function decline.[23] In this Chinese-population-based study, 3768 subjects who were enrolled in an atherosclerosis cohort showed estimated glomerular filtration rate (eGFR) decline with elevated WBC count. The results supported the hypothesis that systemic inflammation may serve as a risk factor for CKD and AKI development.

Our study also showed that ABG results do not have statistical significance to be considered as a good determinant for AKI development. Available studies on the relationship between ABG particularly metabolic acidosis do show that acidosis is an independent risk factor for the development of kidney injury. Hu Jiachiang et al conducted a retrospective study on 4,873

respiratory patients and analyzed their ABG results on admission to determine whether blood gas results are associated with the development of AKI.[24] Their results showed that hypocapnia and metabolic acidosis were both considered predictors of AKI development.

Furthermore, admitting creatinine, creatinine clearance and BUN are all considered determinants of potential AKI development. Multiple studies have shown that creatinine and BUN are prognostic markers for developing renal injury. In a study by Grynberg, Keren et al., 40 out of 196 cardiac patients undergoing elective cardiac surgery were shown to have developed AKI post-surgery.[25] These patients had elevated creatinine and BUN and a lower glomerular filtration rate pre- and post-operatively. This study concluded that creatinine and BUN elevation is associated with the development of AKI, providing a cheap readily available prognostic marker.

Another practical application of AKI prediction is to guide clinicians in deciding when to start renal replacement therapy or hemodialysis. In this study, about one-fifth (21%) of the critically ill patients who developed renal injury had subsequent renal replacement therapy. This is supported by numerous observational studies such as that authored by Liu, Kathleen et al that demonstrated an association between initiation of dialysis with high degree of azotemia and mortality even after adjustment for key confounders and selection effects.[26] In this study, 250 participants who had high BUN and Creatinine on admission received dialysis during their ICU stay.

To summarize, our study illustrated that age, hypertension, atherosclerotic cardiovascular disease, weight, WBC count, creatinine, and BUN are good predictors of AKI among critically ill septic patients. Multiple studies have reported the same findings. Poston et al., cited advanced age, chronic kidney disease, and cardiovascular disease as the risk factors that most consistently led to AKI.[27] Likewise, Malhora, et al, in another multicenter prospective observation study, listed congestive heart failure, hypertension, chronic kidney disease, nephrotoxin exposure, chronic liver disease and sepsis as significant predictors for AKI among the critically ill.[10]

We found that fatality rate was notably high among the septic AKI population with more than half (54%) of patients succumbing to illness while only 45% had significantly recovered. Comparable results can be observed in various studies such as that of Bagshaw et al who reported the association of septic AKI with higher crude in-hospital case-fatality rate compared to non-septic AKI (70.2% *versus* 51.8%).[28] Bagshaw also concluded that the renal function of non-septic AKI patients was more likely to recover and lead to hospital discharge.

Conclusion

The developed risk prediction tool using routinely available variables is found to be fairly accurate to predict the development of AKI among critically ill septic patients. This can aid clinicians to identify high risk population and will provide strategies for prevention, early diagnosis, and treatment.

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