Prevalence and Clinical Profile of Patients with Pregnancy-related Acute Kidney Injury: A Single-Center Retrospective Study

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Abstract

Background: Pregnancy-related acute kidney injury (PR-AKI) is an underdiagnosed yet serious public health obstetric complication with high risk of maternal and fetal morbidity and mortality. Several studies have varied reports as to its incidence since there is no validated diagnostic criteria. As of date, there is a lack in published studies on the prevalence and clinical profiles of PR-AKI in the Philippines.

Objective: To determine the prevalence of PR-AKI and investigate their clinical profiles and outcomes in a tertiary hospital

Methods: This single-center, cross-sectional, retrospective study included all admitted patients with PR-AKI from January 2019 to December 2021. Prevalence was determined and clinical data and outcomes were obtained and analyzed through review of electronic records.

Results: A total of 49 out of 1374 patients had PR-AKI with a prevalence of 3.57% while prevalence of AKI with underlying CKD was 0.22%. The mean age was at 30 ± 6 years and most were primigravid (51.02%). Most of the patients affected had no pre-existing comorbidities (57.14%) and no known maternal comorbidities (59.18%) prior to the admission. The top causes of PR-AKI were pre-eclampsia/eclampsia (53.06%), blood loss (24.48%) and sepsis/septic shock (22.45%) mostly occurring during the third trimester (69.39%). The mean highest creatinine level was at 1.99 ± 2.01 mg/dL. Only 18.37% had oliguria while hemodialysis was done in only 6.12%. ICU admission rates were at 26.53%. Intrauterine fetal demise was seen in 12.24% of cases. PR-AKI had a 6.12% mortality rate. However, most were discharged with normal creatinine (89.8%).

Conclusion: PR-AKI is a serious complication with significant burden even in previously healthy individuals. Prompt diagnosis is essential for a more favorable maternal and fetal outcome as well as improvement of kidney function to baseline.

Keywords: Acute Kidney Injury, Pregnancy, Maternal and Fetal Morbidity and Mortality

Introduction

Background of the Study. Pregnancy-related acute kidney injury is a serious public health obstetric complication with high risk of maternal and fetal morbidity and mortality.[1] Several studies have varied reports as to its incidence due to lack of uniform and validated diagnostic criteria for pregnant patients.[2] There is a disparity between prevalence, causes and outcomes between developing and developed countries.[3] In developed countries, there is a high incidence probably due to higher rates of detection, rise in number of deliveries in hospitals, increase in high-risk pregnancies, and higher rates of overall comorbidities due to advanced maternal age.[1] Acute kidney injury in pregnancy have various etiologies. Most are obstetrical complications while others are common illnesses that just occurred during patient's pregnancy. Its timing during pregnancy may be an important clue as to its underlying cause.[4] Furthermore, there are only a few studies of acute kidney

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injury in pregnancy in Asian countries. Difference in factors such as the climate, socioeconomic status and health practices in Asia are thought to impact its etiology and presentation.[5] As of date, there is a lack of published studies on the prevalence and clinical profiles of PR-AKI in the Philippines.

Significance of the Study. Pregnancy-related acute kidney injury is a relatively uncharted topic in research particularly in the local setting. Furthermore, international data on its prevalence, etiology, risk factors, clinical characteristics, and outcomes on both the mother and the baby are also limited. Information gathered from this study can increase awareness on its significant impact on maternal and fetal morbidity and mortality as well as encourage a more active pursuit in its diagnosis in high-risk individuals to prevent complications particularly on long-term kidney function.

Research Question. What is the prevalence, clinical profiles and maternal and fetal outcomes of patients with pregnancy-related acute kidney injury during the years 2019 to 2022?

General Objective. To determine the prevalence of pregnancy-related acute kidney injury and investigate their demographic profiles and clinical outcomes in a tertiary hospital in Cebu City

Specific Objectives. (1) To determine the prevalence of pregnancy-related acute kidney injury in in a tertiary hospital in Cebu City, (2) To assess the clinical profiles of these patients and identify high-risk individuals, (3) To establish the common causes of acute kidney injury in pregnancy, and (4) To identify outcomes of pregnant patients with this complication

Operational Definitions of Terms

Acute Kidney Injury - KDIGO definition; rise in serum creatinine at least greater than or equal to 0.3 mg/dL within 48 hours or 1.5x from the baseline in the past 7 days

Pregnancy-related Acute Kidney Injury – all pregnant and postpartum patients meeting the increase in serum creatinine criterion of acute kidney injury

Pre-existing comorbidity – disease or medical condition, both congenital or acquired that the patient was diagnosed with prior to pregnancy

Maternal comorbidities - disease or medical condition related to pregnancy

Oliguria - urine output less than 0.5 ml/kg/hr in 24 hours

Methodology

Study design. This study was a single-center, cross-sectional, retrospective chart review including all admitted patients with pregnancy-related acute kidney injury based on elevations of serum creatinine meeting the KDIGO definition.

Study Setting and Time Period. This study was done in a 660-bed capacity, private, tertiary hospital in Cebu City of which the medical records of patients admitted from January 1, 2019, to December 31, 2021 were retrieved and reviewed.

Population and Sampling Frame. The study initially included all admitted obstetric patients from January 2019 to December 2022. Serum creatinine of each of these patients were checked. Patients with only one or no documented serum creatinine as well as those whose laboratory results cannot be retrieved from the system were excluded in the study. Obstetric patients who fulfill the PR-AKI criterion during their admission were identified and their electronic charts were examined.

A total of 3556 obstetric patients were admitted during January 1, 2019 to December 31, 2022. Among them, 2182 patients either had only one or no documented serum creatinine taken during the admission or whose laboratory records were unsuccessfully retrieved in the hospital system and were thus, excluded for the study. Out of the 1374 pregnant patients with at least two documented serum creatinine, only 49 patients fulfilled the KDIGO definition of acute kidney injury (*Figure 1*).

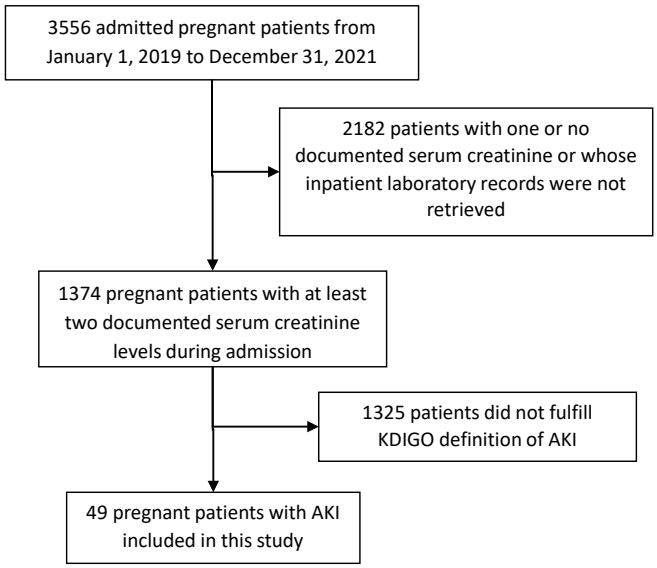

Figure 1. Schematic illustration depicting patient selection for the study

Data Collection. Chart data of the included study population were retrieved from the medical records section of Chong Hua Hospital after approval of the protocol by the Institutional Review Board of our institution. A list of obstetric patients from January 2019 to December 2022 was retrieved. Serum creatinine of each of these patients were checked through the EMR application using the hospital's computer. Patients with only one or no documented serum creatinine as well as

Table I. Prevalence of Pregnancy Related-Acute Kidney Injury (PR-AKI)

Year	Total No. of Pregnant Patients Included	Patients with AKI *n* (%, 95% CI)	Patients with AKI with Underlying CKD *n* (%, 95% CI
2019	512	14 (2.73,1.64, - 4.54]	1 (0.20, 0.03 - 1.10)
2020	275	10 (3.64,1.99, - 6.56]	1 (0.36, 0.06 - 2.03)
2021	284	12 (4.23,2.43, - 7.24]	1 (0.35, 0.06 - 1.97)
2022	303	13 (4.29,2.52, - 7.20]	0 (0.00, 0.00 - 1.25)
Total	1374	49 (3.57,2.71, - 4.68]	3 (0.22, 0.07 - 0.64)

Note: p denotes proportion; CI means Confidence Interval and is determined through the Wilson score interval

Table II. Age of Patients with PR-AKI, n = 49

Characteristics	No. of Patients (%)
Age in years, (Mean ± SD)	30.26 ± 5.97
Age Category	
<20	2 (4.08)
20-29	20 (40.82)
30-39	25 (51.02)
>40	2 (4.08)

Table III. Medical history of Patients with PR-AKI, n = 49

Characteristics	No. of patients (%)
Number of Pre-existing Comorbidities	
None	28 (57.14)
One comorbidity	13 (26.53)
Two or more comorbidities	8 (16.33)
Pre-existing Comorbidities	
Hypertension	8 (16.33)
Diabetes Mellitus	7 (14.29)
Bronchial Asthma	4 (8.16)
SLE	4 (8.16)
Immune Thrombocytopenic Purpura	2 (4.08)
Congenital Heart Disease	1 (2.04)
Hyperthyroidism	1 (2.04)
Hypothyroidism	1 (2.04)
Chronic Glomerulonephritis	1 (2.04)
Number of Maternal Comorbidities	
None	29 (59.18)
One comorbidity	14 (28.57)
Two or more comorbidities	6 (12.25)
Maternal Comorbidities	
Advanced maternal age	9 (18.37)
Gestational DM	8 (16.33)
Gestational HPN	6 (12.24)
Peripartum Cardiomyopathy	4 (8.16)
Subclinical Hypothyroidism	3 (6.12)
APAS suspect	2 (4.08)
Placenta Previa	1 (2.04)
High-Risk Pregnancy	33 (67.35)
Consultation with IM prior to admission	23 (46.94)

those whose laboratory results cannot be retrieved from the system were excluded in the study. Chart and electronic medical records of patients fulfilling the PR-AKI criterion were retrieved and reviewed to obtain their baseline characteristics and clinical data. Demographic data included their age, gravida, and parity. Presence of pre-existing comorbidities as well as illnesses during pregnancy were determined to classify if patient had a high-risk pregnancy. Data pertaining to acute kidney injury such as history of underlying chronic kidney disease, serum creatinine levels during admission, presence of oliguria, cause of acute kidney injury and whether hemodialysis was done were obtained. Obstetric information including number of prenatal visits, stage of pregnancy during the admission and mode of delivery if patient delivered during admission were also acquired. Finally, maternal outcomes including patient mortality as well as latest serum creatinine and need for hemodialysis after discharge for patients who were discharged improved, were recorded. Perinatal outcomes such as mortality and if born alive, the maturity of the baby was noted. The Case Record Form is the main data gathering tool to acquire the information pertinent to this research. It will be filled up by the researcher and encoded into a Microsoft Excel spreadsheet. The case record forms will be stored in a discreet location known only to the researcher. The electronic copy will also be password protected and stored in a secure computer.

Statistical analysis. The incidence per year and prevalence of PR-AKI for four years were elucidated using frequency and proportion together with a confidence interval of the proportion. Descriptive analysis of the baseline characteristics was utilized. Categorical variables were presented using frequencies and percentages. Continuous variables were presented as mean standard deviation.

Results

A total of 49 pregnant patients out of 1374 patients qualified for the study had acute kidney injury for the past four years. The incidence of AKI among pregnant patients was noted to be increasing from 2.73% in 2019 to 4.29% in 2022. The overall prevalence of AKI in patients over the four-year period was 3.57%. The confidence interval suggests that the true prevalence rate of AKI among patients is from 2.71% to 4.68%. The presence of underlying CKD in pregnant patients with AKI remained relatively low, ranging from 0% to 0.36% over the past 4 years. The overall prevalence of AKI with underlying CKD in pregnant patients over the four-year period was 0.22%. The confidence interval suggests that the true prevalence rate of AKI with underlying CKD among patients is from 0.07% to 0.64%. The data indicates that AKI during pregnancy is uncommon, but the presence of underlying CKD in these patients is rare. *Table I* presents the prevalence of Pregnancy-Related Acute Kidney Injury (AKI) over four years. It shows the percentage of pregnant patients who developed AKI each year, along with the percentage of those with underlying chronic kidney disease (CKD).

Table II shows the age of patients with PR-AKI. Most of the patients with PR-AKI are in the 30-39 years (51.02%) and

Table IV. Obstetric history of Patients with PR-AKI, n = 49

Characteristics	No. of patients (%)
Number of Previous Pregnancies	
0	25 (51.02)
1	17 (34.69)
2	4 (8.16)
3	2 (4.08)
4	0 (0.00)
≥5	1 (2.04)
Number of Prenatal Visits	
0	1 (2.04)
1 to 2	5 (10.20)
3 to 4	1 (2.04)
> 5	42 (85.71)
Mode of Delivery	
Did not deliver during admission	10 (20.41)
NSVD	6 (12.24)
Vacuum-assisted VD	3 (6.12)
Emergency CS	22 (44.9)
Elective CS	2 (4.08)
Postpartum	6 (12.25)

Table V. Causes, timing and characteristics of PR-AKI, n = 49

Characteristics	Frequency (%)
Causes of AKI	
Preeclampsia with Severe Features/Eclampsia	26 (53.06)
Sepsis	11 (22.45)
Post-operative AKI secondary to blood loss during Cesarean Section	6 (12.24)
Urinary Tract Infection	4 (8.16)
AGE	4 (8.16)
Postpartum Hemorrhage Secondary to Uterine Atony	3 (6.12)
COVID Confirmed	3 (6.12)
Peripartum cardiomyopathy	3 (6.12)
Abruptio Placenta	3 (6.12)
HELLP Syndrome	2 (4.08)
Rhabdomyolysis	1 (2.04)
Timing of AKI Episode	
First trimester	3 (6.12)
Second trimester	6 (12.24)
Third trimester	34 (69.39)
Postpartum	6 (12.24)
Underlying CKD	3 (6.12)
Highest Creatinine Level, Mean ± SD	1.99 ± 2.01
Highest Creatinine level	
<1.5	30 (61.23)
1.5 to 3	13 (26.53)
3-4.5	3 (6.12)
>4.5	3 (6.12)
Oliguria	9 (18.37)
HD done	3 (6.12)
ICU admission	13 (26.53)

20-29 years (40.82%) age groups with a mean age of 30.26 years with a standard deviation of 5.97 years.

More than half of the patients had no pre-existing comorbidities (55.1%) and maternal comorbidities (53.06%) prior to admission. The most common pre-existing comorbidities are hypertension (16.33%), diabetes mellitus (14.29%), bronchial asthma (8.16%) and systemic lupus erythematosus (8.16%). On the other hand, the most common maternal comorbidities include advanced maternal age (18.37%), gestational diabetes mellitus (16.33%) and gestational hypertension (12.24%). Most of the pregnant patients who had acute kidney injury were considered to have a high-risk pregnancy (67.35%) during their prenatal visits and several had consultations with an internist (46.94%) for control of comorbidities prior to admission. *Table III* presents the medical history of patients with PR-AKI.

Most of the pregnant patients had no previous pregnancy (51.02%) or had only one previous pregnancy (34.69%) before episode of acute kidney injury (*Table IV*). At least five prenatal visits were done prior to admission in 85.71% of the pregnant mothers. Only one patient had no prior prenatal check-up before the admission. The most frequent mode of delivery was emergency cesarean section (44.9%) followed by normal spontaneous vaginal delivery (12.24%) then vacuum-assisted vaginal delivery (6.12%). There were pregnant patients who did not deliver their babies during the said admission (20.41%) and 12.25% presented with AKI in the postpartum period.

The top three causes of AKI in a tertiary hospital for four years were pre-eclampsia/eclampsia (53.06%), sepsis (22.45%) and post-operative AKI secondary to blood loss during cesarean section (12.24%) as seen in *Table V*. Most AKI occurred during the third trimester of pregnancy (69.39%) while only 6.12% presented during the first trimester. Three patients with acute kidney injury had underlying chronic kidney disease comprising 6.12% of the study population. The mean highest creatinine level during the course of the admission was at 1.99 ± 2.01 with most of them only <1.5 mg/dL (61.23%). Only 18.37% of the patients had oliguria while hemodialysis was done in only 6.12% of the patients. Patients who were admitted to the intensive care unit are 26.53% of the study population.

In this study, PR-AKI had a 6.12% mortality rate. However, most had improved kidney function and was discharged with normal creatinine (89.8%). Among the three patients who had hemodialysis, one eventually expired during the admission, one had improved kidney function and hemodialysis was discontinued while the last one continued hemodialysis as outpatient (2.04%). Mean length of hospitalization was 16.45 ± 51.76 days with usual length of hospitalization < three days (30.61%) and four to seven days (28.57%).

Intrauterine fetal demise is seen in 12.24% of cases while most babies were delivered alive (55.10%). Preterm babies comprise of 36.73% including all those who were delivered dead. Live, term babies make up 32.65% of the cases.

Discussion

In this four-year study, pregnancy-related acute kidney injury was noted in approximately 3 in 100 obstetric patients admitted in a single-center tertiary hospital. In a large systematic review and meta-analysis involving 31 studies, PR-AKI had a pooled incidence of 2%.[6] Although there was a noted 164% increase in incidence of PR-AKI between 1999-2001 and 2010-2011 in the United States, an incidence of only 0.81% was demonstrated in an eight-year retrospective study done in a single center in China.[7,8] Differences in incidence of PR-AKI may be due to absence of a standard diagnostic criteria and lack of aggressive work-up reflecting low awareness of its morbidity particularly in developing countries.[1] It should be noted that a total of 2182 out of 3556 admitted obstetric patients with no documented laboratory work-up were excluded in our study.

The mean age of affected patients was at 30 years with only 18.37% categorized as having advanced maternal age. Other studies even had lower mean age of patients with PR-AKI at 26-29 years old.[6-8] Most of the patients affected had no pre-existing comorbidities (57.14%) and no known maternal illnesses (59.18%) prior to the admission. However, 67.35% were classified to have a high-risk pregnancy during prenatal consults. Only 2.04% had no prior prenatal visit and a total of 12.24% with poor prenatal follow-up. Several of these patients were seen by an internist (46.94%) for control of comorbidities prior to admission.

This reflects that PR-AKI typically occurs in healthy young women who had regular antenatal care but acquired pregnancy-related medical conditions.[3,9,10] More than half of the patients in this study are primigravid (51.02%). However, the difference is not substantial enough as to establish it as a possible risk factor while results in other studies are conflicting.[6,11]

The leading cause of PR-AKI in our study was preeclampsia/eclampsia (53.06%) with all having severe features which was consistent with the findings in most literature.[2,3,6,7,12] Clinical risk factors for preeclampsia such as chronic hypertension (16.33%), gestational hypertension (16.33%), Overt DM (14.29%), gestational DM (16.33%), SLE (8.16%), APAS (4.08%), nulliparity (51.02%) and advanced maternal age (18.37%) were found in a significant number of patients included in the study. HELLP syndrome (4.08%), which is often associated with preeclampsia, contributed to PR-AKI at a lesser proportion. Both are multiorgan disease that manifest as edema, hypertension, proteinuria and renal insufficiency among others.[2]

Sepsis from both obstetric or non-obstetric causes was noted to be the second most common etiology of PR-AKI in this study (22.45%) as well as in several other reports.[3,11,12] Hemorrhage in pregnancy including antepartum hemorrhage in abruptio placenta (6.12%), intrapartum hemorrhage due to blood loss during cesarean section (12.24%) and postpartum hemorrhage secondary to uterine atony (6.12%) were significant causes of AKI throughout the stages of pregnancy. Persistent hypotension and disturbances in renal microcirculation including a local reversible inflammatory reaction with tissue ischemia and tubulointerstitial edema may lead to AKI which may progress to tubular cell necrosis and renal cortical necrosis.[13]

Since the timing of our study included the COVID pandemic, a sizeable proportion of the obstetric population had AKI most likely due to COVID-19(6.12%) regardless of severity. AKI as a complication of COVID-19 is associated with severe illness, prolonged duration of hospitalization and poor prognosis in both obstetric and general population.[14] Cardiorenal syndrome secondary to peripartum cardiomyopathy (6.12%) is a rare but significant cause of PR-AKI. Although there is still much left to be elucidated, the renal consequences of this condition are like those occurring in non-pregnant population.[13] Highest creatinine level in our study was at 1.99 ± 2.01 mg/dL with 61.23% having <1.5 mg/dL. Due to absence of standardized definition of PR-AKI, varying serum creatinine level cut-offs were included in different studies.

However, in a similar descriptive study in Nepal, higher mean serum creatinine levels were noted. It was also in this study that oliguria was demonstrated as the most common symptom at diagnosis.[8] Meanwhile, in our study, only 18.37% of the patients had oliguria. Severe AKI prompting hemodialysis occurred in only 6.12% of the cases. On the other hand, two studies from India had rates as high as 70% of obstetric patients with AKI requiring hemodialysis.[3,12]

In this study, most acute kidney injury during pregnancy occurred during the third trimester (69.39%) reflecting pre-eclampsia or eclampsia as well as hemorrhage as frequent causes of AKI. These conditions necessitate emergency delivery of the baby with emergency cesarean section (44.9%) as the most common mode of delivery. Severe blood loss during delivery may also contribute to PR-AKI particularly in the postpartum period.

PR-AKI was associated with significant maternal and fetal morbidity and mortality as demonstrated in several studies.[2-4,6,10] Several pregnant patients had intrauterine fetal demise (12.24%) in this study. A higher percentage of babies born prematurely (36.73%). In a systematic review in Africa, perinatal mortality was high at 1.5-60.5% attributed to limited access to obstetric care and late diagnosis of women at risks for PR-AKI.[13] Although most of the fetal outcomes were favorable, there were higher rates of preterm delivery and low birthweight.[16] (In this study, 26.53% of the patients was admitted to an intensive care unit with a mortality rate of 6.12%. Among the three patients who had hemodialysis, one eventually expired during admission, one had improved kidney function and hemodialysis was discontinued while the last one continued hemodialysis as outpatient. Furthermore, 89.8% of patients with PR-AKI had a normal serum creatinine upon discharge. In most studies, immediate recovery from PR-AKI was more common

while a minority of the patients will progress to end-stage renal disease.[6,11,16]

Limitations. This study was conducted in a single-center private, tertiary hospital and may not represent the general population of the locality. Inherent patient factors and differences in medical practice and resources may also exist. Most of the admitted pregnant patients had one or no documented serum creatinine taken during the admission while outpatient laboratories prior to the admission were not included in the study. This may have eliminated several patients at risk of AKI for monitoring of serum creatinine. Furthermore, there is no established serum creatinine criteria for acute kidney injury in pregnancy. The data used in this study was solely from information retrieved from the electronic chart from the medical records. Lastly, the study also did not consider long-term maternal and perinatal outcomes which can only be observed through outpatient follow-up.

Conclusion

Pregnancy-related acute kidney injury is a serious complication with significant burden even in previously healthy individuals. The overall prevalence of PR-AKI over the four-year duration of the study was 3.57%. It frequently occurs in primigravid women in their third trimester at a mean age of 30.26 years old. Although most patients affected initially had no pre-existing comorbidities, maternal illnesses during pregnancy makes a significant number of these patients have a high-risk pregnancy. The most common pre-existing comorbidities are chronic hypertension, diabetes mellitus and SLE while maternal comorbidities such as advanced maternal age, gestational hypertension, gestational DM and APAS were noted in these patients. The leading causes of AKI in this study were pre-eclampsia/eclampsia, sepsis/septic shock, and hemorrhage. PR-AKI has been associated with significant maternal and fetal morbidity and mortality. Aside from the need for hemodialysis and intensive care unit admission, there is high mortality rate at 6.12%. A considerable number of patients had intrauterine fetal demise and premature birth. Fortunately, improvement of kidney function and a normal serum creatinine was noted in most discharged patients. Prompt diagnosis is essential for a more favorable maternal and fetal outcome as well as improvement of kidney function to baseline.

Recommendations.

This study recommends further investigation with a larger, multi-center study including both private and public hospitals with a longer timeframe to capture a prevalence and clinical profile more representative of the general obstetric population. Close monitoring of serum creatinine and urine output in patients at risk for PR-AKI as well as more aggressive work-up for all possible causes of AKI should be routine so as not to miss out any diagnosis. Future studies may also investigate establishing a validated correlation to risk factors and outcomes of PR-AKI at any stage in the pregnancy and in the postpartum period. Long-term monitoring of kidney function including dependency to hemodialysis should also be pursued.

Funding: Department of Internal Medicine, Chong Hua Hospital

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