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MED840 RESEARCH PROJECT

Research Report

Incidence and Outcome of Acute Kidney Injury at TTM Hospital, Samoa – A Prospective Descriptive Study

By
Nathan Maligi Chadwick
Bachelor of Medicine & Bachelor of Surgery
Fiji School of Medicine
Suva, Fiji
2010

Post Graduate Diploma in Internal Medicine
Fiji National University
Suva, Fiji
2016

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Incidence and Outcome of Acute Kidney Injury at TTM Hospital, Samoa – A Prospective Descriptive Study

Research Project Approval: CHREC; Health and Research Committee Samoa

Assistant Professor Dr Mai Ling Perman

MMED Research Project Adviser

Dr. Folototo Leavai

Co-Supervisor

Dr. Donald Wilson

Course Convener: MED 840, Research Project

Associate Professor Odille Chang

Chair: Postgraduate Advisory Committee, Department of Medical Sciences

Associate Professor Odille Chang

Head of School : Medical Sciences

Associate Professor William May

Dean of the College: Medicine, Nursing & Health Sciences

ABSTRACT

Incidence and Outcome of Acute Kidney Injury in patients admitted to TTM Hospital – A Prospective Descriptive Study

Chadwick N[1], Perman M[2], Leavai F[3]

Researcher Affiliations:

[1]Internal Medicine Unit, School of Medical Sciences, College of Medicine, Nursing and Health Sciences, Fiji National University, Suva; Fiji

[2]Internal Medicine Unit, School of Medical Science, College of Medicine Nursing and Health Sciences, Fiji National University, Suva, Fiji

[3] Medical Unit, Tupua Tamasese Meaole Hospital, Ministry of Health, Apia, Samoa

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Introduction

Acute Kidney Injury (AKI), a common global syndrome, characterized by an acute reduction in the glomerular filtration, is associated with considerable morbidity, mortality and high healthcare cost. The key to reduction of unfavorable outcomes is early detection and early treatment.

There is paucity of data on non-critical care settings particularly from Pacific island countries. This study aims to determine the incidence and outcomes of AKI in adult patients admitted to the general wards of a tertiary referral center in Samoa.

Methods

Using the 2012 KDIGO definition of AKI and a cut off serum creatinine level of >200umol/l, adults admitted to the general wards of this single-center during the 6-months study period were prospectively followed up from admission to 3-months post-discharge.

Data collected was entered into Microsoft Excel 2010 and statistically analysis was done using SPSS.

Results

AKI was diagnosed in 114 patients during the study period from 1st December 2019 to 31st May 2020. Of these, eight five (75%) were community acquired. The mean age was 55.8 years and 57.9% were males. The incidence was 26.8 per 1000 admissions and population based incidence was 1880.9 pmp/year. Dehydration (79%) and sepsis (64%) were the 2 main precipitating factors for AKI in this cohort. More than 40% has 2 or more co-morbidities. The in-patient mortality rate was 20.2%. Out of 91 who were alive on discharge, 25% (23/91) died within 3-months post-discharge, 18.7% (17/91) progressed to chronic kidney disease and only 25% had complete resolution.

Conclusion

This study highlights the high incidence and unfavorable outcomes of acute kidney injury particularly in those who are middle-aged and with co-morbidities. It provides a platform to raise awareness of AKI with the public, government and health care professionals.

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ABBREVIATIONS

AKIN – Acute Kidney Injury Network

AKI – Acute Kidney Injury

ADQI – Acute Dialysis Quality Initiative

CKD – Chronic Kidney Disease

CKD-EPI – Chronic Kidney Disease Epidemiology Collaboration

HDU – High dependency unit

ICU – Intensive care unit

KDIGO – Kidney Disease-Improving Global Outcomes

MOH – Ministry of Health

NKF – National Kidney Foundation

RIFLE – Risk, Injury, Failure, Loss and End-stage

TTMH – Tupua Tamasese Meaole Hospital

GLOSSARY

Incidence – the occurrence, rate or frequency of a disease.

Outcome – the way an event turns out, a consequence.

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CHAPTER 1: INTRODUCTION

1.1 BACKGROUND INFORMATION

Acute Kidney Injury (AKI) is a well-established, frequent, and often under-recognized condition associated with a high mortality, and a nine-fold increased risk of development of chronic kidney disease (CKD), and other organ dysfunction. [1,4] Diagnosis and treatment of AKI are challenging particularly in low resource settings such as Samoa where financial and medical resources are scarce and consequently provision of adequate healthcare is limited for substantial parts of the population. The International Society of Nephrology conducted a "Global Snapshot" about AKI in 2014, where 45% of cases were from low and lower middle-income countries. [23] AKI affects approximately 13.3 million individuals globally per year. An estimated 85% of those affected live in the developing world. AKI is thought to contribute to about 1.7 million deaths every year. [4]

AKI (formerly known as Acute Renal Failure (ARF)) is simply defined as the rapid loss of function of the kidneys. In 2012, Kidney Disease: Improving Global Outcomes (KDIGO) group modified the criteria for diagnosis of AKI by grouping it into 3 stages of increasing severity based on the level of rise in baseline serum creatinine or the decrease in urine output over different time periods.[3]

Table 1: KDIGO definition of AKI

	Serum Creatinine criteria	**Urine output criteria**
Stage 1	1.5–1.9 times baseline **OR** ≥0.3 mg/dl (≥26.5 umol/l) increase	<0.5 ml/kg/h for 6–12 hours
Stage 2	2.0–2.9 times baseline	<0.5 ml/kg/h for 12 hours
Stage 3	3.0 times baseline **OR** Increase in serum creatinine to ≥4.0 mg/dl (≥353.6 umol/l) **OR** Initiation of renal replacement therapy	<0.3 ml/kg/h for 24 hours **OR** Anuria for 12 hours

AKI is a complex disorder that occurs in a variety of settings, especially in critical care, with clinical manifestations ranging from a minimal elevation in serum creatinine to anuric renal failure needing renal replacement therapy. It is often under-recognized and is associated with severe consequences such as end stage kidney disease and death. [4]

The etiology of acute kidney injury can be divided according to the anatomic location of the physiological defect, that is, pre renal, post renal and intrinsic renal. [5]

Pre renal disease involves a disturbance of renal perfusion which can be due to hypotension, hypovolemia or heart failure while **post renal** disease involves obstruction of the urinary collecting system by renal calculi, tumor or stricture. **Intrinsic renal** disease can be further classified according to the component of the kidney that is primarily affected, that is, tubular, glomerular, interstitial or vascular. Acute tubular necrosis is usually caused be ischemia or nephrotoxic agents. Glomerular causes include post infectious and other glomerulonephritis while acute interstitial nephritis can be secondary to medications, infections (bacterial, viral, fungal) or systemic disease (eg.sarcoidosis, lupus). Vascular causes of intrinsic acute kidney injury include renal atheroembolic disease and malignant hypertension. [5]

More than one causative factor may coexist in a patient, and the manifestations and clinical consequences of different causes of AKI can be difficult to distinguish. However, management of AKI is largely dependent on the clinical presentation and the underlying etiology.[5]

Once the etiology is established, specific therapy can be started. Severe acidosis, hyperkalemia, drug intoxication, uremic pericarditis, encephalopathy, or volume overload refractory to medical management mandates the initiation of renal replacement therapy.

Samoa has a population of 195,979 with a median age of 21.4years. Life expectancy for males is 72years and females at 78years. Samoa's expenditure on health is 7.22% of its gross domestic product. [26,27] Samoa's main referral hospital, Tupua Tamasese Meaole Hospital (TTMH) is located in its capital Apia on the main Island Upolu. It has a total bed capacity of 209. It is supported by six district hospitals, four health centers and another hospital on the bigger island of Savaii. The TTM hospital provides primary,

secondary and limited tertiary care. Its overseas treatment scheme is made through collaborations with New Zealand and India's Health Care Systems.

Hemodialysis is the only modality of renal replacement therapy available in Samoa. Acute Hemodialysis is only offered at TTM hospital in the Intensive Care Unit (ICU) and in the High Dependency Unit (HDU) in the general medical ward. Inpatient hemodialysis is fully funded by the government. Should a patient progress to chronic kidney disease requiring ongoing dialysis as an outpatient, this service is provided at the National Kidney Foundation. (NKF) Majority of costs for chronic hemodialysis is again subsidized by the government. The indirect costs dialysis imposes on the families of these patients is still quite burdensome.

The International Society of Nephrology has recognized the gravity of the problem and launched a global human rights initiative, the 0 by 25 Initiative, in 2013 with the aim to eliminate preventable deaths from acute kidney injury by the year 2025. [6] The initiative aims to address this issue by obtaining existing and prospective data to establish AKI via a cross sectional global cohort study; raising awareness of AKI in the worldwide community to reduce variations in management; and developing a sustainable infrastructure to enable needs- based approaches for education and training and care delivery. [6]

1.2 STATEMENT OF THE PROBLEM

Acute kidney injury is a global problem. It has numerous causes which are often preventable and treatable with simple measures. Often inadequate timely management leads to adverse outcomes.

In order to promote prevention strategies and to implement adequate resources for AKI management, it is important to gauge and understand the magnitude of the problem in Samoa.

Although renal replacement treatment option like hemodialysis is available in Samoa, yet there is a great need to develop preventative strategies to reduce the burden on renal replacement therapy resources and facilities.

There is no data on the epidemiology of AKI in Samoa.

The purpose of this study was to determine the incidence of AKI in adult patients admitted to TTM hospital, and to identify the commonest causative factors leading to this syndrome and how they were managed during the admission period.

1.3 AIMS & OBJECTIVES

AIM

The aim of this research is to determine the incidence and outcomes of patients admitted to the medical, surgical, obstetrics and gynecology and the intensive care departments of TTM hospital with acute kidney injury from 1st December 2019 to 31st May 2020.

OBJECTIVES

1. To describe the demographic profile of patients admitted to TTM hospital with a diagnosis of AKI over a 6 months period.
2. To determine the causes of AKI in these patients
3. To identify the various modes of treatment given
4. To determine the outcome of AKI patients in terms of mortality and resolution of AKI

CHAPTER 2: REVIEW OF LITERATURE

Acute kidney injury has a huge global burden with high morbidity and mortality. There have been variable incidence and mortality rates reported in literature depending on many factors. [7]

To begin with, the definition of acute kidney injury (acute renal failure) has changed numerous times with more than 30 different definitions reported in literature before 2004. [8] Acute Dialysis Quality Initiative (ADQI) developed the consensus Risk, Injury, Failure, Loss, and End-stage Kidney (RIFLE) classification of ARF in 2004 which was later modified to the Acute Kidney Injury Network (AKIN) criteria in 2007. That is when the term AKI replaced ARF. As the shortcomings [uses eGFR as part of the definition, does not take into account obstructive causes] of the RIFLE and AKIN criteria were recognized, the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines for AKI published in 2012 proposed a further modification of the RIFLE and AKIN criteria and hence the current diagnostic criteria. [8] Studies were done using different definitions over time and this makes comparison of incidence and mortality difficult.

Moreover, the availability and quality of data on incidence rates of AKI vary depending on the economy of a country, that is, between developed and developing countries but there are limited data available from the latter. [4,9,10] A study by Bagasha et al in Uganda gives a picture of the limitations of research done in a low resource setting. [8] The differences between AKI in a low resource and a high resource setting are important for many reasons and the most important one is that AKI in these settings is potentially more preventable and treatable as most of the patients are quite young with no comorbidities and the only failed organ is the kidney. Tariq et al in a study in UK showed the incidence of AKI as 1811 per million population with a 50% 6 month mortality. [9] In comparison, a study by Jha at et al in India showed an incidence of 6.4 per 1000 admissions. [10] This does not mean that there is low disease burden in India. The paucity of good quality data in this setting is usually due to late presentation to tertiary care centers and lack of resources for lab tests and treatment.

A study by Chandra et al looking at the incidence and outcome of AKI in Fiji showed that the hospital based incidence was 21 per 1000 admissions and the population based incidence was 855 per million population per year. Mortality rate was 43% and there was recovery of kidney function in 59% of patients. [21]

Other factors influencing incidence and mortality are the setting in which AKI is diagnosed, that is, community acquired versus hospital acquired or ICU versus non ICU settings. A study by Hsu et al comparing the Community acquired and hospital acquired AKI in Taiwan showed an incidence of 17.25 per 1000 admissions with 26.07% mortality for community acquired AKI whereas hospital acquired AKI despite having a lower incidence of 8.14 per 1000 admissions had quite a higher mortality of 51.58%. [11] There has been a lot of research done on AKI in ICU. The AKI-EPI study, a multicentre international cross sectional ICU study showed an incidence of 62.5% and increasing mortality with increasing severity of AKI. [12] This study had used the KDIGO defining criteria.

In addition, the population studied, that is, paediatrics versus adults is also an important factor. Two studies in India showed that the incidence of acute kidney injury was 5-9% in pediatric inpatient wards and 25-36% in pediatric intensive care units in 2008 and 2010. [13, 14] Another study in a tertiary care facility in India in 2000 showed AKI in 1.9% of adult patients. [15] Moreover, a meta-analysis carried out using the KDIGO definition showed that 1 in 5 adults (21.6%) and 1 in 3 children (33.7%) experienced AKI worldwide. [9]

It is important to determine the cause of AKI because the initial evaluation and management are tailored to the particular cause. The cause could either be pre-renal, post-renal, or intrinsic.

Pre-renal AKI, caused by under-perfusion of an otherwise normal kidney, accounted for 21% of cases of ARF in a multicenter study in Madrid. [16] The hallmark of pre-renal failure is that it is quickly reversible with appropriate therapy.

Post-renal AKI, caused by obstruction of the urinary tract, accounted for 10% of cases in the Madrid study. [16] Urinary tract obstructions may be within the urinary tract (e.g. blood clots, stones, sloughed papillae, fungus balls), or extrinsic (e.g. pelvic tumors, abdominal tumors, retroperitoneal fibrosis, even inadvertent ligation).

Once pre-renal and post-renal causes are ruled out, intrinsic renal failure is likely. Intrinsic AKI, caused by disease of the renal parenchyma, accounted for 69% of cases in the Madrid study. [16]

According to the paper by Jha et al, the etiology of AKI varies between developed and developing countries. In developed, temperate countries, where the disease burden is dominated by lifestyle-related chronic diseases and degenerative disorders in the elderly, AKI usually occurs as part of multiple organ involvement in an already hospitalized, elderly patient or after surgical or diagnostic interventions, and iatrogenic factors have an important role. [17] However, the causes of AKI in developing tropical countries include infections (leptospirosis, malaria), envenomation; ingestion of toxic herbs or chemicals; poisoning; and obstetric complications. [17]

The study by Ram et al. in 1985 in Fiji had described the causes based on sub-specialties at the time; that is obstetrics, surgical and medical. Majority of the patients had medical causes including leptospirosis, acute glomerulonephritis, paraquat ingestion and miscellaneous (septicemia, hepatorenal syndrome, acute gastroenteritis). [18]

A study done on long-term prognosis after acute kidney injury requiring renal replacement therapy in ICU patients in Geneva showed that among patients who survived an episode of AKI, 10% had developed ESKD at 3.0–3.5 years. Moreover, patients with previous CKD had a 25% incidence of ESKD at 3 years. In addition, the prevalence of CKD was elevated with nearly one in two patients with no known CKD prior to AKI progressing to CKD within 3 years. [19] There is an increased risk of chronic dialysis following a hospitalization complicated by acute kidney injury and dialysis. This is especially so among patients without a preexisting diagnosis of chronic kidney disease. [20]

In the meta-analysis by Susantitaphong et al, the pooled AKI-associated mortality rate was 23.9% in adults and the mortality rate declined over time. Moreover, the mortality rate was inversely related to income of countries and percentage of gross domestic product spent on total health expenditure. [9]

CHAPTER 3: METHODOLOGY

3.1 Study Type/ Methodologies, Data Collection Techniques & Variables

This was a single-centered prospective descriptive study of adults (> 18 years) with a diagnosis of AKI admitted at TTM Hospital, Apia, Samoa from 1st December 2019 – 31st May 2020.

Information gathered from inpatient medical records were entered into a datasheet and the following variables were collected: age, gender, ethnicity, admitting department, whether AKI is community or hospital acquired, baseline creatinine within the preceding 12 months, co-morbidities (diabetes, hypertension, pre-existing CKD, heart failure and chronic liver disease), presenting symptoms, the KDIGO criteria met, the probable causes, urea and creatinine on the day of diagnosis, different modalities of treatment and the outcome in terms of mortality, and recovery of kidney function.

The datasheet is adapted from the datasheet used by ISN for the Global Snapshot project which was a cross sectional, global prospective cohort study designed to better understand the growing burden, identification and management of AKI in different settings worldwide. Please see the datasheet in Appendix 3.

3.2 Sampling

Inclusion criteria

1. Adults aged more than 18 years admitted in TTM Hospital during the study period with a diagnosis of AKI at any time during that hospitalisation.
2. Adults aged more than 18 years admitted in TTM Hospital during the study period with a serum creatinine of >200micromol/L and fulfilled the 2012 KDIGO criteria for diagnosis of AKI.

3. Patients with underlying chronic kidney disease with an episode of AKI were also included in this study.

Exclusion criteria

The following patients were excluded from this study:

1. Patients on chronic haemodialysis
2. Patients with underlying CKD with no evidence of AKI
3. Patients in whom it was impossible to ascertain the diagnosis, that is, those patients with only one-off elevated serum creatinine levels with no subsequent follow up bloods.

3.3 Process for Data Collection

The Laboratory Excel Spreadsheet which is an electronic database of all laboratory investigations accessible to all wards at TTM hospital, was used to get a list of patients with creatinine values greater than 200mircomol/L. This value was used as the cut off in order to make this study comparable to other studies done overseas. Using a cutoff value for creatinine also ensured that all patients on the severe spectrum of the disease were captured. This list was then given to the Records Department for folder retrieval. Patients less than 18 years and those who were treated on an outpatient basis were eliminated. Those with established end stage kidney disease on chronic hemodialysis, or had underlying chronic kidney disease with no evidence of AKI (using KDIGO Criteria) during admission within the study period were also excluded. Information extracted from patient files were recorded onto the datasheet (Appendix 3) which were then entered into Microsoft Excel spreadsheet for analysis.

3.4 Process for Data Management and Analysis

KDIGO definition of AKI was used.[3] Baseline creatinine was established using a value within 365 days before current admission but not during a prior hospitalization.[28] However, if baseline creatinine was not available, creatinine on admission or a value within 3 months of admission, whichever was lower, was used to impute baseline creatinine. Resolution of kidney function was defined as serum creatinine decreased to or below baseline. Follow up of these patients were done 3 months from admission to determine recovery of their kidney function.

Acute kidney injury was regarded as community acquired if the KDIGO criteria for AKI were met on admission whereas hospital acquired AKI was labeled if the KDIGO criteria were met 24 hours or longer after hospitalization.

Data analysis was performed using Microsoft Excel pivot tables and STATA. Survival analysis was done using unadjusted Kaplan Meier curve and comparison of binary variables done using unpaired t-test.

3.5 Ethical Considerations

Ethics approval was sought from the Fiji National University, College Health Research Ethics Committee (CHREC), the Samoa Ministry of Health-Health Research Committee (MOH-HRC) and permission from the Deputy Director General of TTM Hospital before data was collected.

This study was a Prospective Descriptive Study. All information accessed from the patients' folders was kept confidential. Collection was on a de-identified data collection sheet. Identifying patient information with corresponding patient code was only accessible to the primary investigator. The patients themselves were not approached as all information was passively collected from routine hospital records.

CHAPTER 4: RESULTS

4.1 Study Recruitment

During the study period 1st December 2019 to 31st May 2020, there was a total of 1185 patients who had a serum creatinine of more than 200micromol/L. 1071 patients did not meet the inclusion criteria, so 114 patients were included in the study.

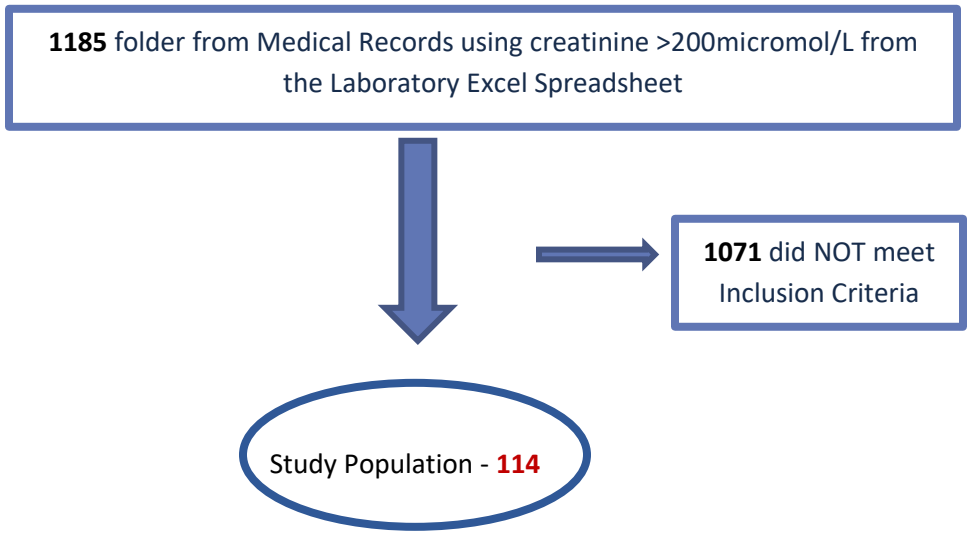


Figure 1: Recruitment of patients in the study

4.2 Demographic and baseline characteristics

The mean age of the patients was 55.8 and 66 (57.9%) were males. One hundred and thirteen (99.1%) were all of Samoan descent with 1 (0.9%) being of Chinese Ethnicity.

Community acquired AKI was identified in 85 (75%) of patients whereas the rest had hospital acquired AKI. Most of the patients were admitted with the Department of Internal Medicine, 91 (80%) followed by the Department of Surgery, 22 (19%) and Department of Obstetrics and Gynecology 1 (0.9%).

Comorbidities identified were Hypertension (47%), Chronic Kidney Disease (43%), Diabetes mellitus type 2 (41%), Heart failure (32%) and Chronic Liver disease (1%). It is also important to note that 43% of patients had more than one co-morbidity, being hypertension, diabetes mellitus, heart failure and chronic kidney disease concurrently.

Table 1: Demographic and baseline characteristics

	Demographics	Total n=114 (%)
Age	Mean age	55.8
Gender	Male Female	66 (57.9) 48 (42.1)
Ethnicity	Samoan Others	113 (99.1) 1 (0.9)
Clinical setting	Community acquired Hospital	85 (75) 29 (25)
Department	Internal Medicine Surgery Obstetrics & Gynecology	91 (80) 22 (19) 1 (0.9)
Comorbidities	Hypertension Chronic Kidney Disease Diabetes Mellitus Type 2 Heart failure Chronic liver disease >2+ comorbidites	54 (47) 49 (43) 47 (41) 36 (32) 1 (1) 49 (43)

Baseline creatinine was not available in 78 patients (68.4%) so it had to be imputed using the creatinine on admission or a value within 3 months of admission, whichever was lower. Of the 78 cases, 59 (75.6%) were community acquired AKI and 19 (24.4%) were hospital acquired.

4.5 Incidence

There was an average of 19 admissions per month with a diagnosis of AKI. This computes to a hospital based incidence of 26.8 per 1000 admissions per 6 months and a population based incidence of 1880.9 per million population per year.

In categorizing patients into increasing order of severity based on the 2012 KDIGO Staging, 60 (52.6%) patients had Stage 1 AKI, followed by Stage 3 AKI with 31 (27.2%) patients then Stage 2, with 23 (20.2%) cases. Since urine output measurements were difficult to ascertain in all the patients the serum creatinine criterion was used for staging of AKI.

Most patients had a combination of precipitating causes identified in figure 2 below. Dehydration was the prevalent precipitating cause of AKI found in 90 (79%) of all cases. Causes of dehydration were poor oral intake in 82 (91%) cases and diarrhea and vomiting found in 8 (9%) cases

Second commonest was sepsis found in 73 (64%) of all cases. Events classified under sepsis included pneumonia, 33 (45.2%), Cellulitis, 15 (20.5%), Diabetic sepsis, 6 (8.2%), gastroenteritis, 5 (6.8%), urinary tract infections, 5 (6.8%), Abscess, 3 (4.1%), and then epididymo-orchitis, leptospirosis, appendicitis and emphysematous pyelonephritis all with 1 (1.4%) case each.

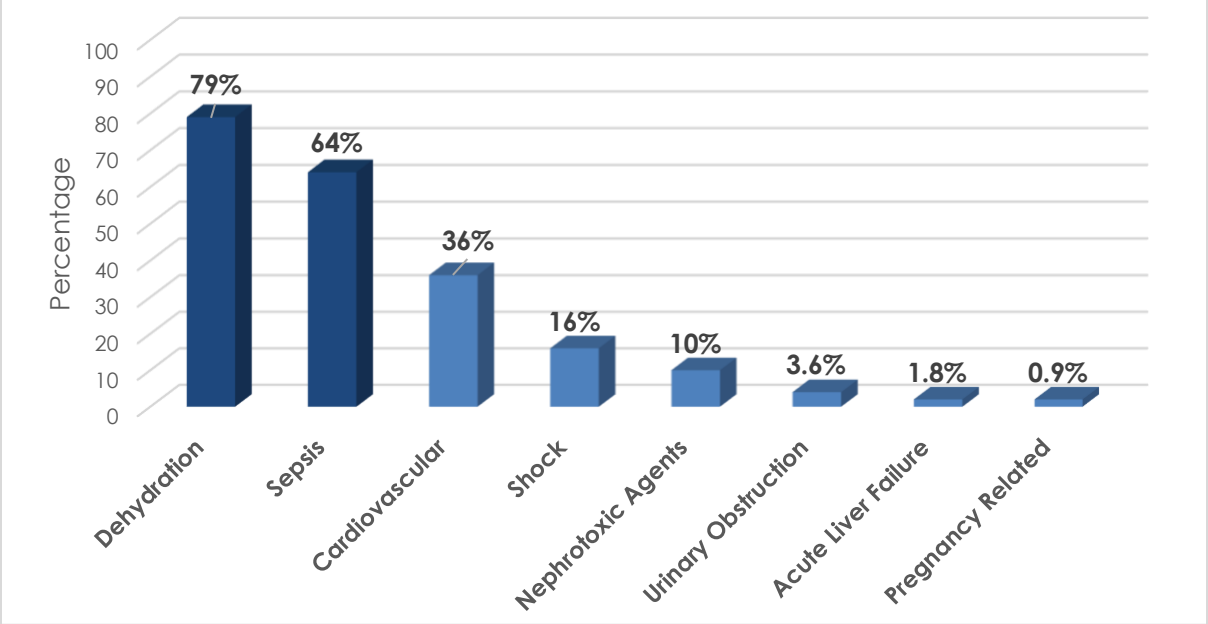
Cardiovascular events accounted for 41 (36%) of cases, with heart failure seen in 31 (75.6%) and acute myocardial infarction in 10 (24.4%) of patients with cardiac as a causative factor of AKI.

Eighteen (16%) patients presented in shock, with septic shock being more common in 14 (77.8%) of cases, then cardiogenic shock, 3 (16.7%) and hypovolemic shock with 1 (5.5%) case due to massive blood loss intra-operatively.

Nephrotoxins were found in 11 (10%) patients where NSAIDs were found in 10 (90.9%) patients and Contrast in 1 (9.1%) case.

Only one patient had pre-eclampsia during pregnancy resulting in AKI.

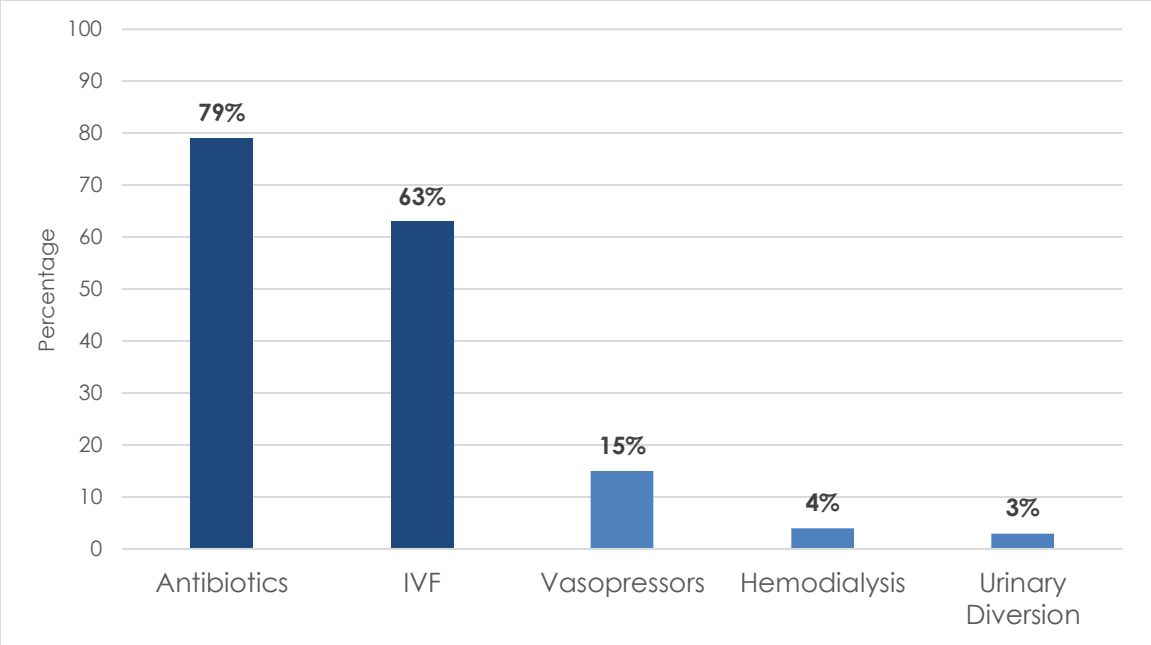
Figure 2: Precipitating Causes of AKI



None of the patients had a kidney biopsy as this procedure cannot be performed in Samoa due to resource constraints (no renal specialist, lack of special stains). Only 79 (69.3%) of cases had a urinalysis done and 69 (60.5%) had an ultrasound scan of the kidneys.

Most patients received a combination of the various treatment modalities: IV Antibiotics, IV Fluids (normal saline fluid), Vasopressors, hemodialysis and urinary diversion. (Figure 3). Only 5 (4%) out of all the patients received acute emergency hemodialysis.

Figure 3: Treatment modality of AKI



It is important to note that some patients presented with sepsis on a background of heart failure and had some dehydration, and were advised on oral hydration measures to reduce the risk of developing pulmonary edema from aggressive intravenous fluid resuscitation.

4.4 Sub analysis of the HD group

Hemodialysis is a major intervention available for patients with AKI. Five (5) patients had intermittent acute hemodialysis using the Fresenius 4008b machine. The average number of days from diagnosis to initiation of dialysis was 2.4 days.

The indications for hemodialysis were electrolyte imbalance or acid base disturbance (4 cases) refractory fluid overload (1 case). It has to be noted that some patients had more than one indication for dialysis

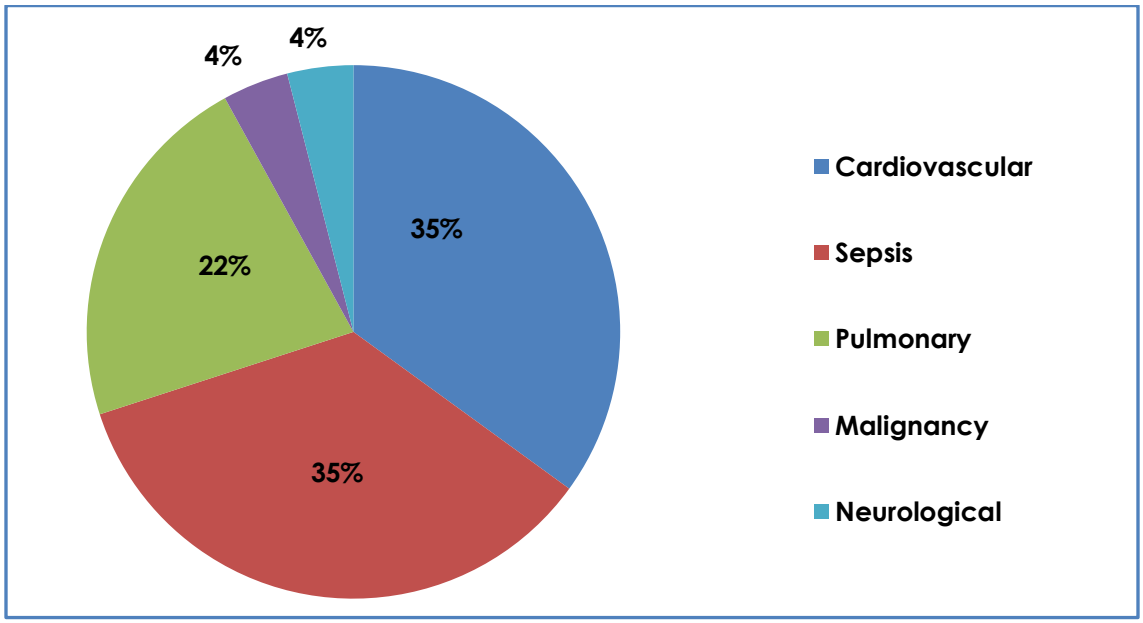
Each patient had an average of 3.8 sessions of HD. Two (2) patients had recovery of kidney function with an average of 16 days to reversal. One (1) patient did not have recovery of kidney function and progressed to ESKD requiring permanent maintenance

hemodialysis. Two (2) patients died while on acute dialysis interventions – 1 died after one session of HD and the other passed away after 8 sessions of HD. The cause of death for both cases were from sepsis.

4.5 Mortality

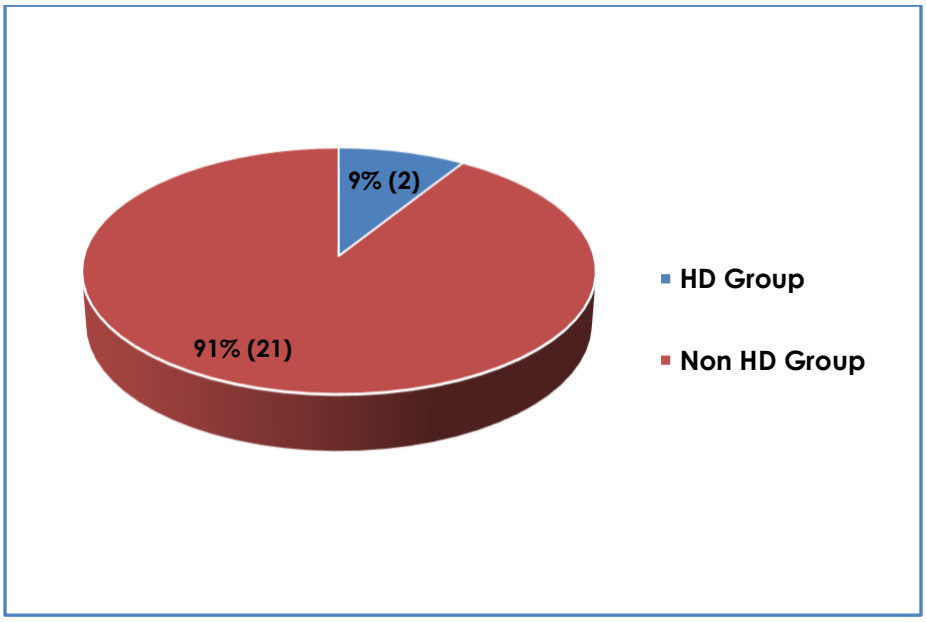
Twenty three patients (20.2%) died during admission; of which 18 (78.3%) had community acquired AKI whereas 5 (21.7%) had hospital acquired AKI. In addition, two (8.7%) underwent hemodialysis. The predominant cause of death as classified in the death certificates were Sepsis and Cardiovascular namely acute myocardial infarction and refractory cardiogenic shock.

Figure 4: Causes of death



Of the 23 patients who died, 2 (9%) had hemodialysis and 21 (91%) did not have hemodialysis intervention. (Figure 5)

Figure 5: Mortality in HD vs Non-HD Group



In further evaluation of the 21 deceased cases who did not have hemodialysis, 14 patients (67%) met indications for acute hemodialysis but the benefit was too futile to be performed given the critical state they were already in. This was taking into account the poor premorbid function of these patients prior to hospitalization, the multiple comorbidities, and the degree of multiple organ dysfunction compounding the overall poor outcome during admission. 7 patients (33%) died and did not satisfy the indication for acute hemodialysis as an intervention.

Figure 6: Mortality in patients where Hemodialysis is Indicated versus Not Indicated

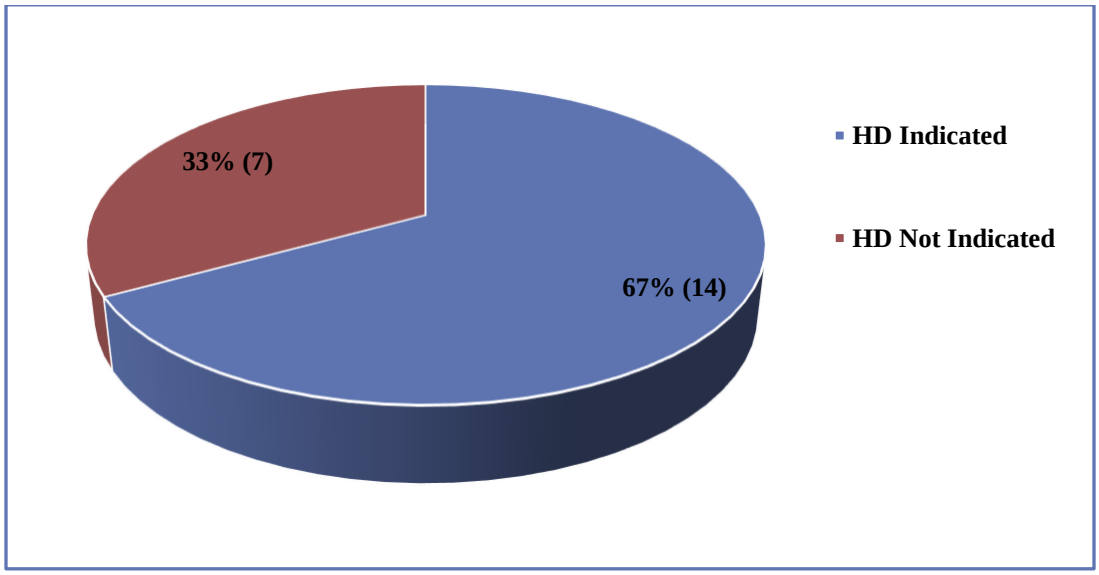
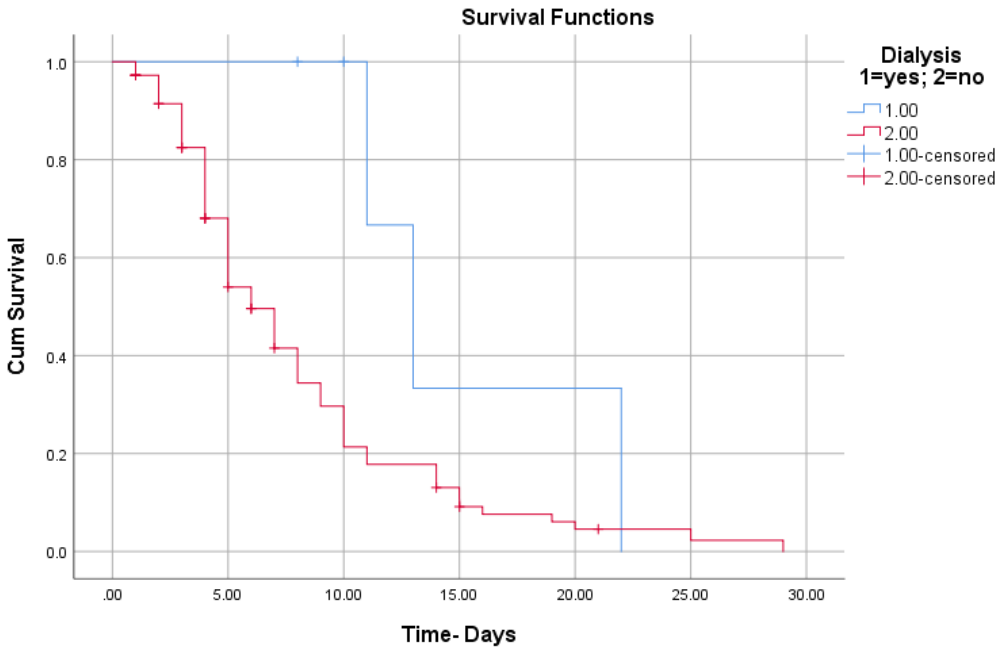


Figure 7: Kaplan Meier survival curve comparing the hemodialysis and non-hemodialysis groups during admission

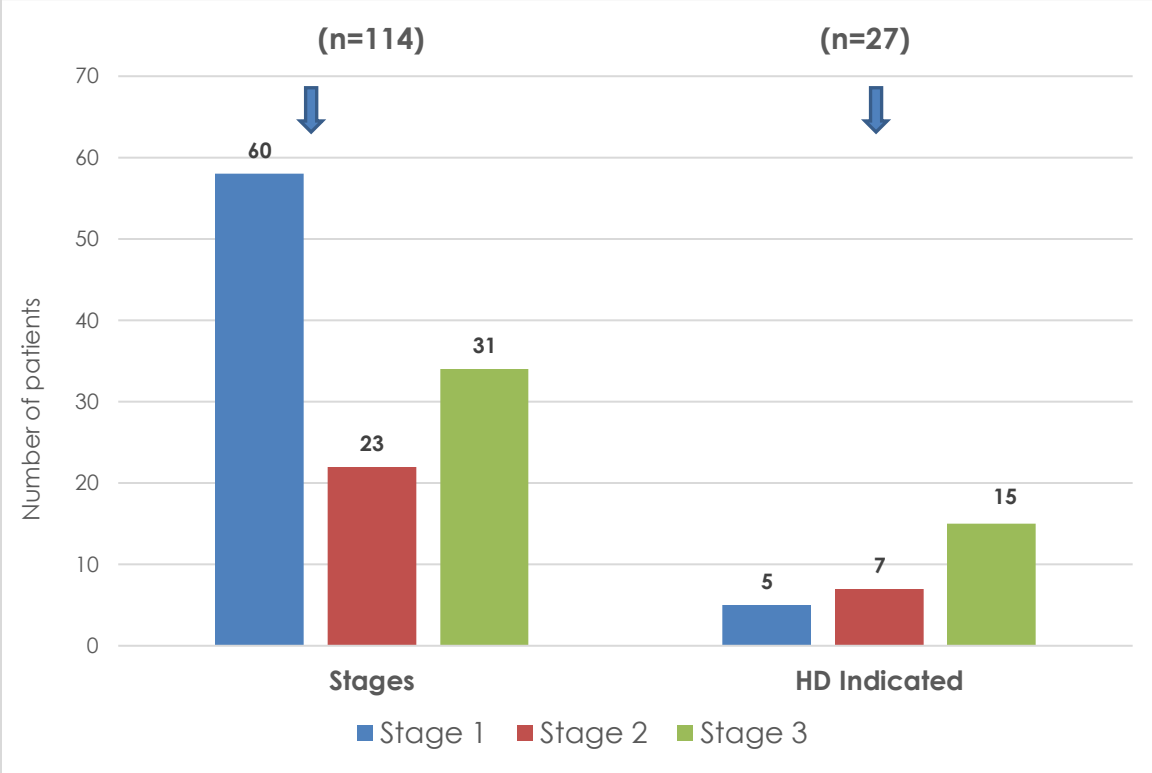


The blue line depicts patients who received hemodialysis whereas the red line represents those patients who did not have hemodialysis. Each drop in the graph represents a patient being censored off due to discharge or lost to follow-up, and each spike or inverted cross signifies death.

For patients who received hemodialysis, they have a median survival time estimated at 13 days (from 9 – 16 days, 95% CI [confidence interval]). For those who did not have hemodialysis their estimated survival time is estimated at 6 days (4.8 – 7 days, 95% CI). This indicates that both groups of patients have poor outcome earlier on in the disease course from around 6 days to 13 days.

It is important to note this survival curve is only calculated from the number of days of admission and not taking into account their progress and survival months or years after discharge. Moreover, it was difficult to determine any beneficial associations of hemodialysis as an intervention to survival due to small number of patients receiving hemodialysis compared to those who did not.

Figure 8: 2012 KDIGO staging for all patients and those who met indications for hemodialysis



Overall, the majority of patients, 60 (52.6%) were in Stage 1, the lesser severe spectrum of the disease, then Stage 3 with 31 (27.2%) patients, then Stage 2 with 23 (20.2%) patients.

Twenty seven (27) patients out of the entire study population met indications for hemodialysis, 5 (16%) in Stage 1, 7 (26%) in Stage 2 and 15 (58%) in the severe spectrum at Stage 3. Only 5 patients (19%) received hemodialysis, and all of them were in Stage 3. Of the 27 cases, 12 patients (44%), hemodialysis was considered futile and more harmful rather than beneficial and 10 cases (37%) refused hemodialysis interventions.

Table 3: Resolution of AKI

Deaths 23 (20.2) Alive on Discharge 91 (79.8)	n=91 (Percentage)
Lost to follow up	5 (6%)
Died within 3 months	23(25%)
Died in Hospital	10
Died at Home	13
No Resolution of AKI	40(44%)
Known CKD	26
De-novo cases	14
AKI Resolution	23 (25%)

Resolution of AKI occurs when serum creatinine decreases to or falls below baseline. Follow up of these patients were done 3 months to 6 months from admission to determine recovery of their kidney function. Patient information system and Laboratory Electronic Excel Spreadsheet were used to identify patients during follow up.

91 (79.8%) patients were discharged after their index admission. 23 (25%) patients died later within 3 months of admission. 10 cases were readmitted and later succumbed in hospital either from sepsis or cardiovascular causes as identified on death certificates. 13 cases died at home within 3 months of discharge. These cases were identified from patient information system when relatives presented to hospital to claim the death certificates. Of the 91 cases discharged, 40 (44%) did not have resolution of their AKI; 26 (65%) cases were known to have pre-existing CKD, either had deteriorating kidney function or progressed to end stage kidney disease. About a third 14 (35%) were de-novo cases (no kidney disease before admission) and only a quarter (25%) had resolution of their AKI.

Five (6%) cases were lost to follow up.

CHAPTER 5: DISCUSSIONS

This prospective descriptive study was the first of such to be performed in Samoa and sought to describe the hospital based incidence, clinical characteristics and outcomes of AKI at TTM hospital and as a result illustrates the magnitude of the problem at a tertiary referral hospital.

The majority of patients presenting to TTM hospital with AKI were in the middle aged group and suffered multiple comorbidities. With the high prevalence of NCD's in Samoa we can predict that this problem would occur. This is similar for AKI in developed or high income countries. On the contrary the AKI Global Snapshot study reveals AKI is more common in the younger population with none or no comorbidity in the low to lower middle income countries (LLMIC). Community Acquired AKI is more common which is supported by studies of AKI in LLMIC countries.[23] The high number of cases noted with the Department of Internal Medicine is likely due to recognition of AKI and documentation by the department. Moreover with sepsis and dehydration being the commonest causes of AKI, both ailments are admitted and treated under the Internal medicine physicians.

The incidence of 26.8 per 1000 admissions (that is 2.7%) is high and comparable to data from Australia where AKI accounted for 1.6% of hospitalizations. [29] Hospital based incidence was calculated using the total number of admissions for the respective departments during the study period. The population based incidence was calculated using the population of Samoa from the 2016 Census. It was difficult to get an age range of > 18 years from the reported census data as it was reported in 5 year ranges, so > 15

years range was used for calculations. Additionally, in order to obtain per million population per year, the value was multiplied by 2 as the study period was 6 months.

Formula:

$$\frac{\text{Sample size}}{\text{Total Pop Samoa} > 15 \text{ years}} \times 1{,}000{,}000 \times 2$$

It is well known that sepsis in any given setting is a common cause of AKI. In this study, both Dehydration and Sepsis were leading causes at 79% and 64% respectively. This is quite high in comparison to the 16.3% sepsis as a cause of AKI found by Bagasha et al in Uganda.[8] Similar leading causes were also identified by Chandra et al in Fiji in 2015 with sepsis causing 62% and dehydration 47% of cases.

Hemodialysis is considered a lifesaving treatment for patients suffering from kidney disease, however only 4% of the study population received hemodialysis. Furthermore, out of the 27 patients who met indications for hemodialysis only 16% proceeded with hemodialysis. Nevertheless, this treatment modality was deemed futile in some of the cases, however, this study did not look at behaviors, attitudes and beliefs of most patients and families in regards to hemodialysis as a treatment option. Perhaps this can be a subject for future studies.

Mortality rate of 20.2% is similar to the global mortality of 23%. [23] as well as a study in Uganda, a low resource setting with a mortality of 21%. [11] as opposed to a higher mortality in Fiji in a study in 2015 by Chandra. Mortality in the hemodialysis group was high at 40%, which is appalling when compared globally with a dialysis associated

mortality at 17%. [23] This could be attributed to the fact that all 5 patients who received hemodialysis were in Stage 3 of AKI while majority of non-dialysis patients were in stage 1 of AKI. The decision to initiate dialysis in AKI is very subjective as shown in a study by Thakar et al [30]. There is a tendency to initiate early dialysis in those individuals who are more severely ill despite its beneficial effects in these patients being unclear.

25% of patients showed complete recovery of their kidney functions, almost similar to a 30% complete recovery and 37% partial recovery in the AKI Global Snapshot study. [23] 44% of patients from this study never recovered from their AKI episode and actually progressed in their kidney disease to a worse stage as alluded to by studies that AKI increases the risk of CKD 9 folds.

CHAPTER 6: CONCLUSION

Acute kidney injury has a high incidence in Samoa especially amongst the middle aged population with comorbidities. The most common causes of AKI are frequently associated with volume responsive “pre-renal” dehydration and sepsis, thus simple inexpensive interventions such as oral hydration and fluid therapy with early sepsis identification and appropriate treatments to prevent AKI may result in a substantial reduction in AKI incidence and severity. This emphasizes the importance to focus much efforts and research on diagnostic tools, risk recognition and protocols to immediately treat with simple approach such as fluid resuscitation, avoiding the need for dialysis.

In this study full recovery of AKI was seen in only 25% of cases whereas 44% had no resolution of AKI, rendering it a major risk factor for progression to chronic kidney disease and ESKD. In the light of high costs of renal replacement therapies, it is clear that AKI prevention is often the only realistic way to decrease its severe impact on morbidity and mortality and health costs.

CHAPTER 7: LIMITATIONS OF THE STUDY

Limitations encountered in this study:

- This study was a single center study for a short duration and therefore may affect the generalizability of results (may not be representative of the whole country)
- By using a Creatinine cut off of >200micromol/L meant that less severe cases were excluded (we could have missed cases along the less severe spectrum of the disease)
- Baseline serum Creatinine was difficult to ascertain as majority of this cohort did not have previously recorded serum creatinine levels on our hospital records as well as on the laboratory system to compare with.
- Poor Coding of Diagnosis of AKI into Patient Information System making it difficult to extract data on patients admitted with AKI
- During the study there was a 3 week period (6^{th} April 2020 – 27^{th} April 2020), when creatinine reagent was out of stock – therefore not able to determine cases during this period.

CHAPTER 8: RECOMMENDATIONS

1. This study shows that there is a high Incidence of AKI at TTM Hospital in Samoa amongst the middle aged with comorbidities:
    - Strengthen NCD Screening and Management to address this population at risk of AKI if become unwell or sick with infections.
2. Educate people on timely presentation to hospital for management given the high number of community acquired AKI, anecdotally patients presenting late to hospital.
3. Review Guidelines and Protocols in the Emergency/Outpatient setting to better identify and resuscitate patients early (using Sepsis Bundles/Guidelines) especially patients coming in with sepsis and dehydration. So that we can minimize the risks of AKI and further deterioration.
4. Increase awareness amongst Health care workers regarding AKI – to have a low threshold for identifying AKI and becoming vigilant and proactive in monitoring and management of AKI in a timely manner, especially for frontline health workers in Emergency and Outpatient Departments as well as the Medical Ward.
5. To improve on patient information system for easier data retrieval
6. Adopt the ISN 0 by 25 Initiative and work towards eliminating preventable deaths from AKI by 2025
7. Improve and strengthen follow up appointment system through establishing a Renal Clinic and having a Renal Specialist to oversee care and optimal management of these patients.

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APPENDICES

Appendix 1: Ethics Approval

College Human Health Research Ethics Committee (CHREC)
Fiji Institute of Pacific Health Research (FIPHR)
College of Medicine Nursing and Health Sciences
Fiji National University (FNU)
Hoodless House, Brown Street, Suva PH: (679) 323 3403

20th November, 2019

Nathan Chadwick
Student ID: s050235
School of Medical Sciences

Subject: Full Approval of your research project proposal.

Title of Research	Incidence and Outcome of Acute Kidney Injury at TTM Hospital, Samoa – A Prospective Descriptive study
CHREC ID	117.19
Primary Investigator (s)	Nathan Chadwick
Supervisor(s)	Dr. Mai Ling Perman, Dr. Folototo Leavai
Co - Supervisor(s)	

Dear **Nathan Chadwick,**

Thank you for your application for ethics review of your research project proposal.

I am pleased to advise you that CHREC has granted **FULL APPROVAL** for your above-mentioned study.

Please note that the following conditions apply to this approval. Failure to abide by these conditions may result in suspension or discontinuation of approval and/or disciplinary action.

i. **Changes to approved research proposal**: The researcher cannot make any changes to the approved research project proposal without making a formal application to CHREC for further consideration.

ii. **Duration of Approval** – approval is granted for the duration of project as outlined in the approved research proposal. If the study cannot be completed on time as planned, the researcher must apply to CHREC for an extension by sending an email to CMNHS-RCO@fnu.ac.fj explaining the reasons and attach a progress report.

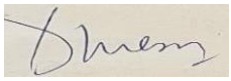
iii. **Adverse events reporting**: Any adverse events that occur shall be reported immediately by the researcher to CHREC.

iv. **Monitoring:** CHREC monitors all research activities after approval is granted.

v. **Final Report**: You must submit a final report at the end of the project by completing the **Final Report Form.**

If you have any further queries on these matters or require information, please do not hesitate to contact the secretariat on email: CMNHS-RCO@fnu.ac.fj or telephone: (679) 323 3403

Yours sincerely



Dr. Donald Wilson
Chair
College Health Human Research Ethics Committee

APPENDIX 2:

Please address
all correspondence to the
Chief Executive Officer

Government of Samoa
Ministry of Health

Office of the Chief Executive Officer
Private Mail Bag, Motootua
Tel: (685) 23330
or 68100 ext 102
Facsimile: (685) 26553

Dr. Nathan Chadwick
Fiji National University
College of Medicine, Nursing & Health Sciences
School of Medical Sciences
FIJI

19 November 2019

Subject: "Incidence and Outcome of Acute Kidney Injury at TTM Hospital, Samoa – A Prospective Descriptive Study" Research

Dear Dr. Chadwick,

Thank you for your request for ethics approval to conduct your research, *"Incidence and Outcome of Acute Kidney Injury at TTM Hospital, Samoa – A Prospective Descriptive Study."* Thank you for your interest in researching health issues. The Health Research Committee (HRC) Secretariat supports your undertaking as the results will contribute to improve acute kidney services at the hospital.

The HRC Secretariat has assessed and evaluated your research proposal and is pleased to inform you that your ethics application has been approved.

Please note the following conditions apply to your research ethics approval. *Failure to adhere to these conditions may result in suspension or termination of approval and/or disciplinary action.*

i. **Duration of Approval** – approval is granted till the duration of the research study as outlined in your research proposal. If for some reason you cannot complete the study in the time frame given, you will need to inform the Health Research Committee by submitting a progress report and stating the reasons for the delay.
ii. **Variation to the Research Project** – any changes or modifications to your research study must be communicated to the Chair of the Health Research Committee for reassessment and approval.
iii. **Monitoring** – your research project is subject to monitoring at any time by the HRC.
iv. **Memorandum of Agreement** – a MoA needs to be signed between your good self and the Ministry of Health (MoH) before you can undertake your research. Please liase with Quandolita Reid-Enari of the HRC Secretariat to organize matters prior to the signing of the MoA.
v. **Final Report** – You must submit a final report at the conclusion of your research project.
vi. **Publication of Findings** – Your final report should not be published without the prior consent of the MoH

Should you require further information/clarification, please do not hesitate to contact Quandolita Reid-Enari or Unaite Asi on telephone 68106 or email: QuandolitaE@health.gov.ws or UnaiteA@health.gov.ws at the Strategic Policy, Planning and Research Division.

We wish you all the best with your research.

Sincerely

Leausa Samau T. Dr. Take Naseri
DIRECTOR GENERAL OF HEALTH /CHIEF EXECUTIVE OFFICER
CHAIRPERSON – HEALTH RESEARCH COMMITTEE

PATIENT DEMOGRAPHICS		
NHN…….. **.** **Age …….**	**Gender** ☐ Male ☐ Female	
Ethinicity ☐ Samoan ☐ Others	**Team patient admitted under** ☐ Medical ☐ Surgical ☐ O&G	**Where was AKI acquired** ☐ Community ☐ Hospital
Which of the following risk factors for AKI does the patient have?		
☐ Age> 75 ☐ DM ☐ Chronic liver disease	☐ Chronic heart failure ☐ CKD ☐ Anemia-Hb<9g/dL	☐ None ☐ Unknown
Baseline serum creatinine within previous 12 months: _____micromol/L		
Which of the following symptoms did the patient present with to suspect AKI (select all that apply)		
○ Dehydration ☐ Diarrhea ☐ Vomiting ☐ Increased thirst ☐ Decreased intake	○ Urinary symptoms ☐ oliguria ☐ polyuria ☐ dysuria ☐ blood in urine ☐ incontinence ☐ urolith passed	○ Swelling ☐ Anasarca ☐ Face and neck ☐ Upper limbs ☐ Lower limbs ☐ Others ……..
○ Hypotension ☐ Low BP(MAP<65) ☐ Shock (use of vasopressors) ☐ Hemorrhage	○ Pregnancy and delivery related symptoms ☐ PV bleeding ☐ Coma ☐ Seizures ☐ Others	☐ Fever ☐ Traumatic injury(indicate site)…… ☐ Allergic reaction(specify)…… ☐ Poisoning (specify)……

Which of the AKI criteria does the patient meet?

- ☐ Increase in serum creatinine by 0.3mg/dL(26.5 micromol/L) or more within 48 hours **or**
- ☐ Increase in serum creatinine to 1.5 times baseline or more within the last 7 days **or**
- ☐ Urine output less than 0.5 mL/kg/h for 6 hours

CLINICAL DATA

Which factors may have contributed to patient's AKI(select all that apply):

Dehydration ☐ Diarrhea ☐ Vomiting ☐ Polyuria ☐ Decreased intake	Liver ☐ Hepatorenal syndrome ☐ Cirrhosis ☐ Acute liver failure	Cardiac ☐ Acute MI ☐ VHD ☐ Heart failure ☐ Pulmonary embolism ☐ Infective endocarditis ☐ Cardiorenal syndrome
Hypotension and shock ☐ Cardiogenic shock ☐ Hemorrhage ☐ Sepsis ☐ Drug induced ☐ Anaphylaxis ☐ Post partum ☐ Hypotension of unclear cause	Acute kidney diseases ☐ Acute Glomerulonephritis ☐ Interstitial nephritis ☐ Pyelonephritis ☐ Rhabdomyolysis ☐ Intravascular hemolysis	Urinary obstruction ☐ Stone ☐ Tumor ☐ Prostate condition
Infections ☐ Leptospirosis ☐ Dengue ☐ TB	Pregnancy related ☐ Miscarriage with septic shock ☐ Puerperal sepsis	Systemic diseases ☐ Multiple myeloma ☐ SLE ☐ DIC

☐ Other bacterial……. ☐ Other viral	☐ Pre eclampsia ☐ PPH ☐ Hyperemesis gravidarum	
Nephrotoxic agents ☐ ACEI/ARB ☐ NSAIDS ☐ Aminoglycosides ☐ Chemotherapy ☐ Contrast	Poisoning ☐ Yes ☐ No	
Blood parameters on the day AKI was confirmed		
Urea ☐ …….. umol/L ☐ N/A	Creatinine ☐ ……umol/L ☐ N/A	Urine output in past 24 hours ☐ …….mls ☐ N/A
Does the patient have a known infection? ☐ Yes …….indicate site…….. ☐ No		
Mark all other organ failures: ☐ Pulmonary ☐ Cardiovascular ☐ Hepatic ☐ Hematologhical ☐ Neurological ☐ None	**Has a urinalysis been done?** ☐ Yes ☐ No ☐ Unknown	**Has a renal scan been done?** ☐ Yes ☐ No ☐ Unknown
DIAGNOSIS AND TREATMENT		
Select the following non dialytic treatment received by patient at the time AKI was diagnosed?		
Fluid therapy	Diuretics	Vasopressors

□ Yes □ No □ Unknown	□ Yes □ No □ Unknown	□ Yes □ No □ Unknown
Antibiotics □ Yes □ No □ Unknown	Urinary diversion (percutaneous nephrostomy,cystectomy or urethral catheterization) □ Yes □ No □ Unknown	Fluid restriction □ Yes □ No □ Unknown
Others (specify)…….		
Has the patient received any dialysis? □ Yes □ No	**Select the indication for starting dialysis** □ Fluid overload □ Symptomatic uremia □ Electrolyte or acid base disturbance □ Intoxication/ poisoning □ Others	
Number of days from diagnosis of AKI to initiation of hemodialysis?		
Which hemodialysis machine was used?.....		
Blood access for hemodialysis □ Femoral □ Internal jugular		
How many sessions of hemodialysis did the patient have in total?.....		
How long (days) did the kidney take to reverse?.....		

What was the average number of hours for each session of dialysis?.....

Was there any fluid transfused during the dialysis?

- ☐ Yes
- ☐ No

Was there any blood transfusion given during the dialysis?

- ☐ Yes
- ☐ No

Blood parameters on the day dialysis was started

Urea	Creatinine	Urine output in past 24 hours
☐ ……umol/L ☐ N/A	☐ ……umol/L ☐ N/A	☐ ……mls ☐ N/A

OUTCOME

Outcome of the patient

- ☐ Alive
- ☐ Deceased

If patient died, what was the cause of death?

☐ kidney failure	☐ hemorrhage	☐ trauma
☐ infection/sepsis	☐ pregnancy related	☐ poisoning
☐ cardiovascular	☐ liver failure	☐ systemic illness
☐ shock	☐ pulmonary condition	☐ malignancy
☐ dehydration	☐ neurological	☐ unknown

Was an autopsy performed?

- ☐ Yes
- ☐ No
- ☐ Unknown

If alive, was the patient scheduled for a follow up in the next 3 months?

- ☐ Yes
- ☐ No
- ☐ Unknown