Study Protocol

Review of Trend in Incidence and Characteristics of Hospital-acquired Acute Kidney Injury in Hospital Selayang

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Table of Contents

List of Abbreviations 3
Research Synopsis 4
1.Background and Significance 5
2. Objective 5
2.1 General Objective 5
2.2 Specific Objectives: 5
3. Methodology 6
3.1 Study Type and Design 6
3.2 Study Population 6
3.3 Inclusion Criteria 6
3.4 Exclusion Criteria 7
3.5 Withdrawal Criteria 7
3.6 Study Outcomes 7
3.7 Sample Size 7
3.8 Study Duration and Timeline 8
3.9 Study Visits and Procedures 8
3.10 Statistical Analysis Plan 8
3.11 Risk and benefit to study participants 8
Benefits to the participants 9
3.12 Risk Benefit Assessment 9
3.13 Ethics of Study 9
3.14 Informed Consent/Assent Process 9
3.15 Privacy and Confidentiality 9
3.16 Conflict of Interest 9
3.17 Publication Policy 9
3.18 Termination of Study 10
References 10

List of Abbreviations

AKI	Acute Kidney Injury
CA-AKI	Community-acquired Acute Kidney Injury
HA-AKI	Hospital-acquired Acute Kidney Injury
ICU	Intensive Care Unit
SCr	Serum creatinine

Research Synopsis

Study title	Review of Trend in Incidence and Characteristics of Hospital-acquired Acute Kidney Injury In Hospital Selayang
Study Population	Patients admitted into Hospital Selayang from: • 1st July 2001 to 30th June 2002 • 1st July 2006 to 30th June 2007 • 1st July 2011 to 30th June 2012 • 1st July 2016 to 30th June 2017
Study Design	Retrospective Cohort Study
General Objective	To investigate the incidence, risk factors and outcomes of Hospital-acquired Acute Kidney Injury in Hospital Selayang over 15 years (5-yearly trend)
Specific Objectives	• To determine the incidence pattern of Hospital-acquired Acute Kidney Injury in Hospital Selayang • To study the determinants associated with development of Hospital-acquired Acute Kidney Injury in Hospital Selayang • To describe the survival outcomes of admissions with Hospital-acquired Acute Kidney Injury, admissions with Community-acquired Acute Kidney Injury and admissions without Acute Kidney Injury in Hospital Selayang
Study endpoints/outcomes	Completion of data collection at the end of the study duration
Sample Size	170000 (minimum 11345 required)
Study Duration	1 year

1.Background and Significance

Acute kidney injury (AKI) is a common problem globally which imposed heavy illness burden to the healthcare system, especially in developing countries. (1, 2) AKI can occur in the community (termed as Community-acquired AKI (CA-AKI)) or in the hospital setting (termed as Hospital-acquired AKI (HA-AKI)). Studies have associated HA-AKI as a preventable disorder, and linked HA-AKI with several immediate and long-term outcomes adversely, such as length of hospitalization, morbidity, and residual renal function. (1, 3, 4) Moreover, delayed recovery to baseline kidney function after AKI episode is found to be associated with higher risk of adverse events and mortality. (5) The impact of HA-AKI is significantly profound, especially among HA-AKI survivors who lost their residual renal function, and remain dialysis dependent. (6)

There was an increasing trend in HA-AKI incidence among hospitalized patients.(6-8) This could be attributed to increased exposure to potentially preventable risk factors during hospitalization. (6) However, studies pertaining to Asian countries are scarce, especially Malaysia. Preventative strategies against HA-AKI could be formulated based on understanding of risk factors which could be identified earlier upon hospital admission. (4)

The purpose of this study is to compare the incidence trend of HA-AKI in Selayang Hospital for the past 15 years, as well as to determine characteristics predictive of such cases. Understanding of clinical variables associated with HA-AKI could facilitate strategies and approaches to prevent, recognize HA-AKI early and mitigate the disease burden of HA-AKI in future.

2. Objective

2.1 General Objective

To investigate the incidence, characteristics and outcomes of Hospital-acquired Acute Kidney Injury in Hospital Selayang over 15 years

2.2 Specific Objectives:

- To determine the incidence pattern of Hospital-acquired Acute Kidney Injury in Hospital Selayang
- To study the determinants associated with development of Hospital-acquired Acute Kidney Injury in Hospital Selayang

- To describe the survival outcome pattern of admissions with Hospital-acquired Acute Kidney Injury, admissions with Community-acquired Acute Kidney Injury and admissions without Acute Kidney Injury in Hospital Selayang

3. Methodology

3.1 Study Type and Design

This is a retrospective cohort study involving 5-yearly trend from 2002 to 2017 for analysis. Laboratory serum creatinine (SCr) results of all patients admitted during study period will be retrieved from the hospital Laboratory Information System. A preliminary screening list will be generated by using STATA program from the SCr results. The nephrologist will then determine HA-AKI as per inclusion and exclusion criteria. Data collectors will collect all relevant data from these patients.

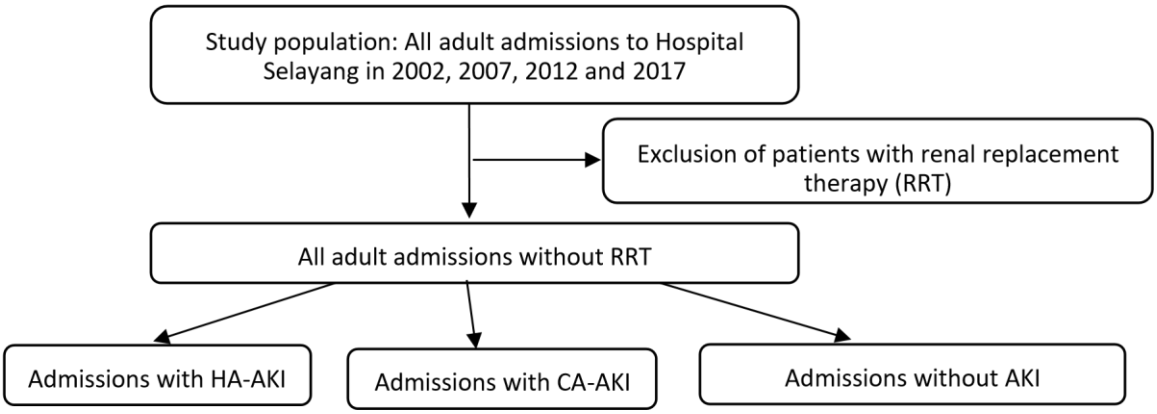

Figure 1. Flow chart of the study

3.2 Study Population

Patients admitted into Hospital Selayang from

- 1st July 2001 to 30th June 2002
- 1st July 2006 to 30th June 2007
- 1st July 2011 to 30th June 2012
- 1st July 2016 to 30th June 2017

3.3 Inclusion Criteria

a) Age of 18 and above at time of hospital admission
b) HA-AKI is defined by any patient who developed AKI (as per definition below) after 48 hours of hospital admission.

c) Definition of AKI(9):

i. An increase in serum creatinine of 0.3 mg/dl (26.5 μmol/l) within 48 hours *OR*
ii. An increase in serum creatinine to more or equal to 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days

d) Definition for baseline creatinine(9):
i. The baseline creatinine level is defined as the creatinine level at or within 7 days before the hospital admission, OR
ii. at the hospital admission OR
iii. the lowest creatinine (excluding the post dialysis creatinine if dialysis is initiated) during the index hospitalisation for those whose baseline creatinine were unknown.

3.4 Exclusion Criteria

o End Stage Renal Failure and on Renal Replacement Therapy (HD, PD or Renal Transplant)

3.5 Withdrawal Criteria

Not applicable

3.6 Study Outcomes

1. Incidence of Hospital-acquired AKI at our centre during study period
2. Renal recovery at 90 days after AKI diagnosis
   Definition for renal recovery:
   a. Full recovery: Return of serum creatinine to or below baseline or within 20% of baseline creatinine
   b. Partial recovery: Serum creatinine remaining 20% above the baseline, but below 50% of the baseline and not dialysis dependent or if previously requiring dialysis and now is dialysis Independent.
   c. Failure to recover: Serum creatinine remains 50% above the baseline or dialysis dependent.

3. In-hospital mortality (from date of AKI diagnosis until date of death in hospital)

3.7 Sample Size

The primary outcome of interest is development of HA-AKI during admission at our centre. The incidence of Hospital-acquired AKI at our centre at March 2017 was 1.19% based on one ongoing study (A prospective, multicenter, observational study to determine the incidence and outcome of Acute Kidney Injury among hospitalised patients in Malaysia). The nine variables to be investigated for predictors of HA-AKI are age, gender, ICU

admission, race, nephrotoxin use, diabetes mellitus, hypertension, congestive heart failure and chronic obstructive pulmonary disease. With an estimation of 15 events per predictor, a minimum of 135 events would be needed, translating to a minimal of 11345 patients at our centre required for the study. The study population fits the minimum sample size requirement as 170283 adult admissions were recorded in total (22788 for Year 2002, 41731 for Year 2007, 46330 for Year 2012 and 59434 for Year 2017).

3.8 Study Duration and Timeline

Proposed study will be conducted from 1 November 2017- 1 November 2018 in the stages shown below:

- Stage 1, review of medical records – 5 months
- Stage 2, data collection and data analysis –5 months
- Stage 3, presentation and publication – 2 months

3.9 Study Visits and Procedures

No study visits and follow up is required as this is a retrospective study through utilisation of existing patient records for data collection.

3.10 Statistical Analysis Plan

The analyses will be performed using IBM SPSS Statistics for Windows (Version 23.0. Armonk, NY: IBM Corp.). Descriptive statistics will be utilized for selected variables. The results will be presented as frequencies and percentage for Categorical Data. Numerical Data which is normally distributed will be presented as mean and standard deviation while median and interquartile range will be presented for Numerical Data which is not normally distributed.

Comparing Numerical Data which is normally distributed between two groups will be analysed using the Independent t-test while Mann-Whitney test will be used if not normally distributed. Multiple logistic regression will be used to study association between risk factors (Numerical Data/Categorical Data) and outcome (Categorical Data). The survival analyses and survival curves from the date of diagnosis until death will be performed using the Kaplan-Meier method, to estimate the index hospitalisation survival rate. All probability values will be two-sided and a level of significance of less than 0.05 (p-value < 0.05) will be considered as statistically significant.

3.11 Risk and benefit to study participants

As this is a retrospective data collection of the participants, no intervention, procedure or treatment will be imposed to the participants during the whole course of the study. Thus, there is minimal risk to the participants.

Benefits to the participants
This study does not present any direct benefit to the participants. However, understanding of HA-AKI patterns at our centre will help in formulating preventative strategies related with HA-AKI.

3.12 Risk Benefit Assessment

As stated above, there is no risk from this study. Study findings shall potentially greatly improve treatment outcomes. The expected benefit outweighs the minimal risk to subjects and thus this study should be supported.

3.13 Ethics of Study

Study will be conducted in compliance with ethical principles outlined in the Declaration of Helsinki and Malaysian Good Clinical Practice Guideline.

3.14 Informed Consent/Assent Process

Not applicable. Consent waiver is permitted from Medical Research Ethics Committee, Ministry of Health Malaysia for this retrospective study and there are no additional study procedures/visits pertaining to this study. Participants' data will be de-identified as there is no collection of personal, identifiable data.

3.15 Privacy and Confidentiality

Subject's names will be kept on a password-protected database and will be linked only with a study identification number for this research. The identification number instead of patient identifiers will be used on subject data sheets. All data will be entered into a computer that is password protected. On completion of study, data in the computer will be copied to CDs and the data in the computer erased. CDs and any hardcopy data will be stored in a locked office of the investigators and maintained for a minimum of three years after the completion of the study. The CDs and data will be destroyed after that period of storage. Subjects will not be allowed to view their personal study data, as the data will be consolidated into a database.

3.16 Conflict of Interest

The investigators declare they have no conflict of interest.

3.17 Publication Policy

No personal information will be disclosed and subjects will not be identified when the findings of the survey are published.

3.18 Termination of Study

The study is anticipated to be terminated at November 1, 2018. The investigators may decide to terminate the study at an earlier date, with written notification given to Medical Research Ethics Committee.

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