

## A retrospective cohort study on unscheduled admissions among patients with end stage renal disease (ESRD) receiving maintenance renal replacement therapy (RRT) and its mortality outcome

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### Abstract

**Background:** While international data exists on hospitalisation and its associated mortality among end-stage renal disease (ESRD) population on maintenance renal replacement therapy (RRT), local data is not known. The objective of this single centre retrospective observational study is to determine the burden of hospital admission and readmission among the ESRD population and the mortality outcome after hospitalisation.

**Methods :** We obtained our study data from the HSNI Batu Pahat nephrology service inpatient database, patients' medical records and Jabatan Pendaftaran Negara (JPN) registry of death.

**Results :** There were 195 index admissions identified from January to June 2016. We found that hospital readmission rate was high at 19.5% within 30 days, 34.4% within 60 days, and 44.6% within 90 days of discharge. Commonest reason of admission was fluid overload (20.7%). Overload was also the commonest reason of readmissions within 30 and 60 days (28.9% and 23.8% respectively), whereas vascular access related issues were the commonest reason of readmission within 90 days of discharge (21.8%). The 90-day mortality rate after index admission was also high at around 18%. The commonest cause of mortality was Infection and Sepsis (42.9%), followed by Acute Coronary Syndrome (22.9%).

**Conclusions :** This study demonstrated the heavy burden of hospitalisation and high mortality rate among ESRD populations. Further larger researches are welcomed to look into the factors associated and the problems faced, in order to improve not only individual morbidity and mortality outcomes, but also on hospitalisation cost and healthcare resources.

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**Keywords :** ESRD on RRT, Hospital Admission, Readmission, Mortality after Hospital Admissions, Reasons of Admission, Reasons of Readmission, Reasons of Mortality

### Introduction

It is common to encounter end-stage renal disease (ESRD) patients admitted to the hospitals. The US Renal Data System (USRDS) report highlighted that the rates of hospital readmissions for ESRD patients are twice those in the general medical population.<sup>1</sup> These admissions have significant impact in terms of costs and length of hospital stay.<sup>2</sup> The readmission rate of this group of population is very high at 34.6% within 30 days of discharge from hospital.<sup>1</sup> The mortality outcome of these patients is also found to be about 20% within 90 days of discharge.<sup>2</sup> While the Malaysian Dialysis and Transplant Registry (MDTR) captures the burden of ESRD in Malaysia<sup>3</sup>, the hospitalisation characteristics, and its morbidity and mortality of ESRD patients are not known. The funding of dialysis in Malaysia has been analysed<sup>3</sup> but to date, the financial and economic impact of hospitalisation among ESRD patients in this country is not studied.

This study aims to determine the burden of hospital admissions among ESRD patients receiving maintenance RRT. We are interested to study the characteristics of admissions, readmissions, and mortalities in this group of population.

### Materials and Methods

The Hospital Sultanah Nora Ismail Batu Pahat (HSNI Batu Pahat) Nephrology Service Inpatient Database is a password protected database and could only be accessed by authorised personnel in the nephrology unit. This database captures all the hospitalised patients who have been referred to the nephrology unit. The database contains the following information:

- Patients' demographic characteristics
- Date of admission and discharge
- Reason of admission and the diagnosis
- Nephrology diagnosis
- Brief summary of patients' progress in the ward
- Date of death and cause of death (if passed away in hospital)

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We identified patients in the above database who were admitted to HSNI Batu Pahat during January to June 2016, with follow up period of 90 days after index admission. Thus, we analysed the database until the end of September 2016, ninety days after the last patient was recruited at the end of June 2016. We included ESRD patients with unscheduled admissions and who were on maintenance RRT. We excluded non-ESRD patients, patients who were not on maintenance RRT, and patients with scheduled admissions (e.g. admission for an elective imaging procedure).

Demographic characteristics (age, gender, race), traceable co-morbidities, date of admissions and discharges, length of stay (LOS), reasons of admission, reasons of readmissions, dates and causes of death (if passed away in hospital) were extracted from the database. When further information was required, patients' medical notes were traced from the HSNI Batu Pahat Medical Record Unit, reviewed, and returned.

While the HSNI Batu Pahat Nephrology Service Inpatient Database captured inpatient mortality, there were patients who died at home or in other hospitals. Thus, we officially contacted Jabatan Pendaftaran Negeri Johor (JPN of Johor state), and through the Registry of Death, we obtained our studied populations' survival status, their dates of death and causes of death.

Data collected were categorised. Numerators and denominators were determined, followed by calculation of percentages of individual causes of admissions, readmissions and mortality. Readmission rates and mortalities rates were calculated by dividing the numbers of readmissions (and mortalities), by the number of index admissions. Cumulative event rates for 30-day, 60-day and 90-day were analysed and plotted.

Mean values of "days to readmission" and "days to mortality" were calculated by dividing the total number of "days to readmissions" (and "days to mortality"), by the total number of readmissions (and mortalities).

## Results

There were 195 index admissions (195 patients) identified from January to June 2016 which met our study criteria. The demographic data is shown in Table 1. Mean age was  $58.5 \pm 13.3$  yrs. The majority of these patients were on maintenance haemodialysis (89.2%) as the mode of RRT. Table 2 shows some of the traceable important co-morbidities of these patients.

**Table 1:**

Demographic Data of 195 patients from HSNI Batu Pahat

| N = 195             |     |            |
|---------------------|-----|------------|
|                     | No. | Percentage |
| <b>SEX</b>          |     |            |
| Male                | 98  | 50.3%      |
| Female              | 97  | 49.7%      |
| <b>ETHNICITY</b>    |     |            |
| Malay               | 148 | 75.9%      |
| Chinese             | 42  | 21.5%      |
| Indian              | 3   | 1.5%       |
| Others              | 2   | 1.0%       |
| <b>MODE OF RRT</b>  |     |            |
| Haemodialysis       | 174 | 89.2%      |
| Peritoneal Dialysis | 18  | 9.2%       |
| Transplant          | 3   | 1.5%       |
| <b>AGE GROUP</b>    |     |            |
| 19 or below         | 1   | 0.5%       |
| 20 – 29             | 9   | 4.6%       |
| 30 – 39             | 10  | 5.1%       |
| 40 – 49             | 28  | 14.4%      |
| 50 – 59             | 47  | 24.1%      |
| 60 – 69             | 65  | 33.3%      |
| 70 – 79             | 31  | 15.9%      |
| 80 or above         | 4   | 2.1%       |

Mean Age  $58.5 \pm SD 13.3$

**Table 2:** Important co-morbidities of 195 patients from HSNI Batu Pahat

| Co-morbidities   | No. | Percentage |
|--|-----|------------|
| Hypertension   | 175 | 89.7%      |
| Diabetes   | 152 | 77.9%      |
| Lower Limb Amputations<br>(Including Toe/Ray's Amputations)      | 62  | 31.8%      |
| Ejection Fraction < 50%<br>from Echocardiogram                   | 54  | 27.7%      |
| Coronary Artery Disease<br>(evidence from coronary<br>angiogram) | 33  | 16.9%      |
| Cerebrovascular Accident   | 17  | 8.7%       |

### Admissions and Readmissions

The mean length of stay (LOS) for index admissions was  $6.6 \pm 7.7$  days while LOS for readmissions was  $6.4 \text{ days} \pm 6.5$  days. Reasons of admissions and their percentages are shown in Table 3. Common reasons of admissions were fluid overload (20.5%), vascular access related issues (16.9%), pneumonia/other respiratory tract infections (RTI) (13.3%), and Acute Coronary Syndrome (ACS) (12.8%). The term Fluid Overload in this study comprised conditions in which there were volume overload regardless of etiologies (e.g. heart, kidney, liver, acute pulmonary oedema, compliance issue to fluid restriction, under extraction, ultrafiltration failure etc). Vascular access related issues included arteriovenous fistula/graft (AVF / AVG) thrombosis, infection, aneurysm, bleeding, and dialysis catheter dysfunctions, excluding catheter related blood stream infection (CRBSI), which is a standalone reason for admission in our study.

**Table 3:** Reasons of admissions and their percentages

| REASONS OF ADMISSIONS (N=195)   |       |      |   |      |     |
|---------------------------------|-------|------|---|------|-----|
| Fluid Overload                  | 20.5% | (40) | Anaemia                                 | 3.6% | (7) |
| Vascular Access Related Issues  | 16.9% | (33) | BP Related Issues                       | 3.1% | (6) |
| Pneumonia/RTIs                  | 13.3% | (26) | Fractures/Dislocations/ Spine Pathology | 2.1% | (4) |
| ACS                             | 12.8% | (25) | Electrolyte Issues                      | 1.0% | (2) |
| Other Infections                | 6.7%  | (13) | Hypo/Hyperglycaemia                     | 1.0% | (2) |
| Skin and Soft Tissue Infections | 6.2%  | (13) | CVA                                     | 1.0% | (2) |
| CRBSI                           | 4.1%  | (8)  | Others                                  | 3.1% | (6) |
| GIT Disorders                   | 4.1%  | (8)  |   |      |     |

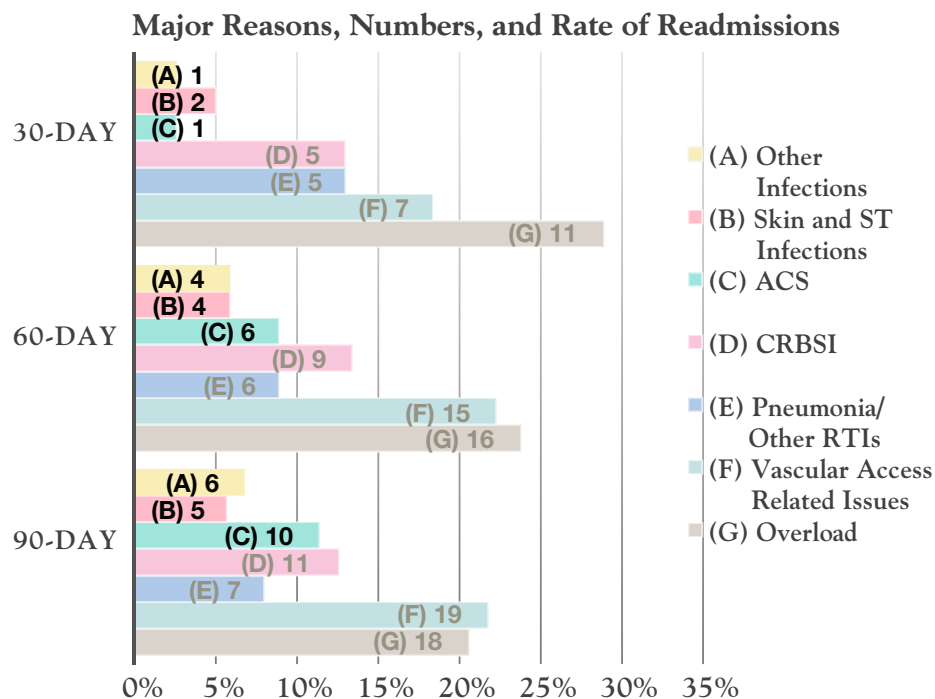
CRBSI – Catheter-related blood stream infection; CVA – Cerebrovascular Accident; *GIT Disorders* – Gastrointestinal Tract Disorders; *BP Related Issues* – Blood Pressure Related Issues)

There were 195 index admissions (195 patients) in the studied period. These index admissions resulted in 38 (19.5%) readmissions within 30 days (30-day readmissions) after discharge from index admissions. The mean days to 30-day readmission was  $12.2 \pm 7.2$  days. Common reasons of 30-day readmissions were fluid overload (28.9%), vascular access related issues (18.4%), pneumonia/other RTI (13%) and CRBSI (13%).

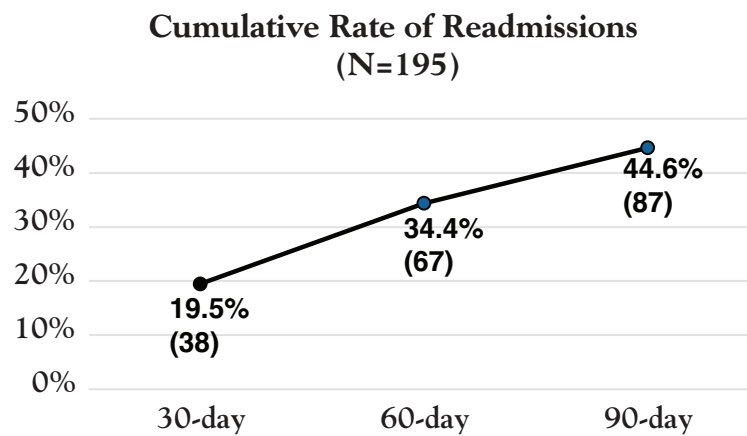
There were 67 (34.4%) readmissions within 60 days (60-day readmissions) after discharge from index admissions. The mean days to 60-day readmission was  $25.9 \pm 17.5$  days. Common reasons of 60-day readmissions were fluid overload (23.8%), vascular access related issues (22.3%), CRBSI (13.4%), pneumonia/other RTIs (8.9%) and ACS (8.9%).

There were 87 (44.6%) readmissions within 90 days (90-day readmissions) after discharge from index admissions. The mean days to 90-day readmission was  $37.3 \pm 26.1$  days. Common reasons of 90-day readmissions were vascular access related issues (21.8%), fluid overload (20.6%), CRBSI (12.6%) and ACS (11.4%). Most of the readmissions (87%, 75 out of 87) did not move to different diagnosis from their index admissions. Figure 1 shows the major reasons and percentages of 30-day, 60-day, and 90-day readmissions while Figure 2 demonstrates the cumulative event rate of 30-day, 60-day, and 90-day readmissions.

When an index admission resulted in more than one readmission, these readmissions were all counted as our readmission of interest. For example, if a patient was readmitted on day 15 and day 55 after index admission, these two readmissions would contribute to one 30-day and one 60-day readmissions.



**Figure 1:** The major reasons and percentages of 30-day, 60-day, and 90-day readmissions. From top to bottom are the readmission rates within 30, 60 and 90 days. The alphabets A-G indicate different reasons of admissions, the number next to the alphabets in the bar chart indicate the number of readmissions.



**Figure 2:** Cumulative readmission rates within 30, 60, and 90 days after discharge from index admission.

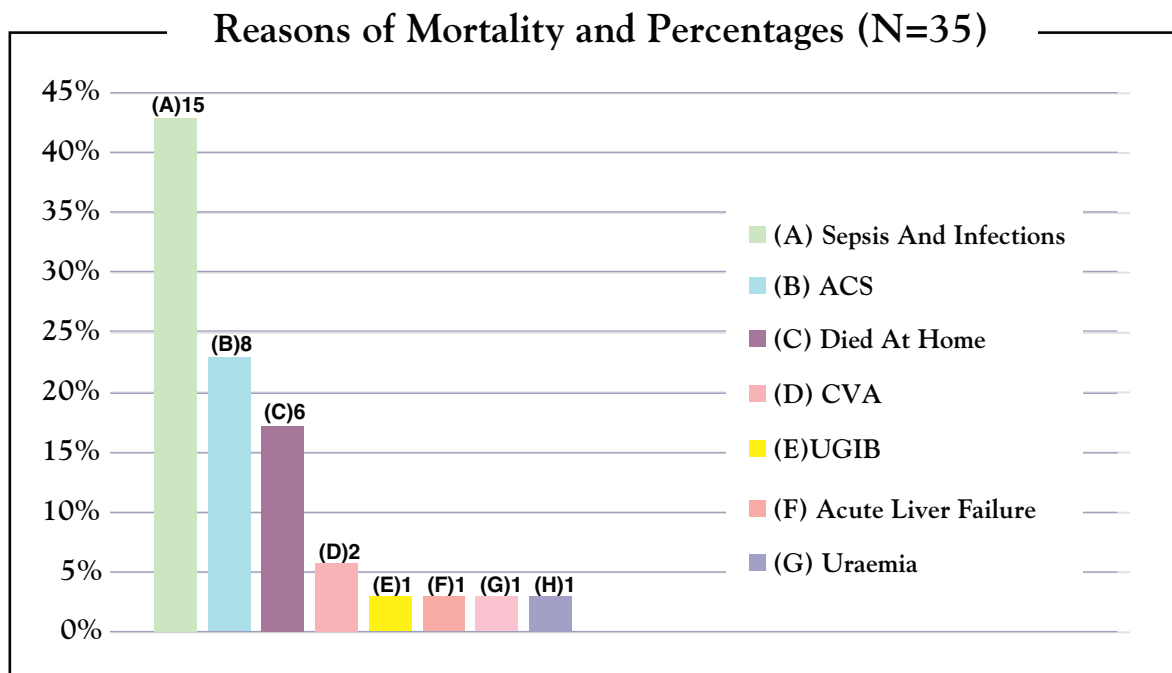
It may be possible that patients were readmitted to other hospitals and these readmissions were not captured in our study. We realised this limitation. However, it is worth stating that 96% of the studied population resided in the Batu Pahat district.

### Mortality

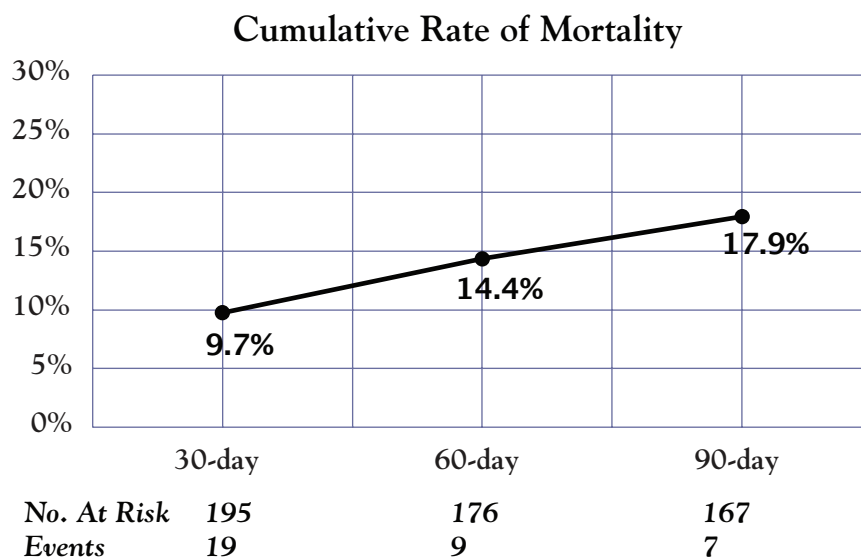
Thirty-five patients died within 90 days after index admissions. The mortality rate within 30 days, 60 days, and 90 days after index admissions (30-day, 60-day, and 90-day mortality rates) were 9.7%, 14.4%, and 17.9% respectively with the mean days to mortalities being  $8.3 \pm 6.4$  days,  $19.8 \pm 19.2$  days, and  $30.7 \pm 28.4$  days respectively. Common causes of death within 90 days after index admissions were Infection and Sepsis (42.9%), ACS (22.9%), followed by 17.1% of them who died at home with the cause of death not determined

by medical personnel. Figure 3 showed the reasons and percentages of mortalities within 90 days while Figure 4 demonstrated the cumulative event rate of 30-day, 60-day, and 90-day mortalities.

Other than the six patients (17.1%, N=35) who died at home, the remaining twenty-nine mortalities occurred in hospital. Out of the twenty-nine in-hospital mortalities, nine occurred during index admissions (25.7%, N=35) and 20 during readmissions (57.1%, N=35). Patients who died at home or during readmissions have a mean LOS of 12.3 days  $\pm$  9.8 days during their index admissions, which seemed to be longer than the mean LOS for overall index admissions ( $6.6 \pm 7.7$  days).



**Figure 3:** Reasons of mortality within 90 days of and their percentages. The text boxes on top of each bar indicate the reasons of mortality in alphabetical label, and the number next to the alphabets are the absolute numbers of deaths observed.



**Figure 4:** Cumulative mortality rates within 30, 60, and 90 days after index admissions.

## Discussion

### **Renal Transplant Probably Has Lower Hospitalisation Rate**

The population on renal replacement therapy (RRT) was 36,611 in Malaysia by 31<sup>st</sup> December 2014.<sup>4</sup> The population on haemodialysis (HD), peritoneal dialysis (PD) and renal transplant were 31497 (86%), 3270 (8.9%), and 1844 (5%) respectively.<sup>4</sup> The demographic data in our study showed that the percentage of hospitalised ESRD patients on HD, PD and renal transplant were 89.2%, 9.2%, and 1.5% respectively. While the US data pointed that hospitalisation rates for HD, PD, and renal transplant patients were 1.7, 1.6 and 0.8 admissions per patient year respectively<sup>1</sup>, local data is scarce. It is possible that renal transplant in Malaysia carries the lowest hospitalisation rate among all RRT modalities, but further research involving more centres would be useful.

### **Fluid Overload Ranks First Among Reasons of Admissions**

Fluid overload was the commonest reason for admissions (20.5%) in our studied population. The etiologies behind fluid overload in ESRD patients are multifactorial, including compliance issue of fluid restriction, excessive salt intake, incorrect dry weight, under-extraction, ultrafiltration failure, loss of residual renal function, heart failure, liver failure, etc. Being said as the commonest reason of hospital admissions in this study, fluid overload was found to be associated with increased mortality<sup>5,6</sup> and more hospitalisations in ESRD populations<sup>7,8</sup>. Fluid overload in dialysis population was also associated with hypertension requiring more antihypertensive use<sup>9,10</sup>, malnutrition, hypoalbuminaemia, inflammation<sup>11</sup>, dialysis-associated hypotension, heart failure, left ventricular hypertrophy and other adverse cardiovascular sequelae<sup>12,13</sup>. Therefore, optimal fluid status management and achieving target dry weight are crucial not only for individual mortality and morbidity purpose, but also for hospitalisation cost and health care resources.

### **High Readmission Rate with Vascular Assess related Issues**

Readmission rates were high at 19.5%, 34.4%, and 44.6% within 30, 60, and 90 days respectively after discharge from index admission. While our data showed a lower 30-day readmission rate of 19.5% compared to US data of 30%<sup>1</sup>, the 90-day readmission rate was striking, translating that almost one in every two hospitalised ESRD patients would be readmitted to hospital again within three months. While fluid overload was still the commonest reason for 30-day and 60-day readmissions, vascular access related issues became the top reason for 90-day readmissions. Vascular access is the “life-line” of ESRD patients on haemodialysis. Worldwide, nephrologists are struggling for the principle of “fistula first, catheter last” due to a better outcome associated with arteriovenous fistula than the other vascular accesses<sup>14,15</sup>, and significant healthcare spending in managing complications associated with different vascular accesses<sup>14</sup>. In our study, vascular access related issues included arteriovenous fistula/graft (AVF/AVG) thrombosis, infection, aneurysm, bleeding, and dialysis catheter dysfunctions, excluding catheter related blood stream infection (CRBSI), which is a standalone reason for admission in our study. Notably, CRBSI contributed only 4.2% of all index admissions but became the 3<sup>rd</sup> commonest reason of 30-day, 60-day, and 90-day readmissions (around 13%). Our study demonstrated that vascular assess related issues and CRBSI tend to be unsolved or recurrent throughout 30, 60, and 90 days. Vascular assess related issues also exceeded fluid overload as the commonest reason for 90-day readmissions, urging further research on vascular access characteristics and problems faced in our local settings.

### **High Mortality Rate with Infection and Sepsis**

The mortality rate within 30 days, 60 days, and 90 days after index admissions were 9.7%, 14.4%, and 17.9% respectively, translating to the fact that almost one in every five hospitalised ESRD patients would die within 90 days after admission to hospital. This 90-

day mortality rate was similar to US data of 20%<sup>2</sup>. The commonest causes of mortality within 90 days in our study were Infection and Sepsis (42.9%), ACS (22.9%), followed by 17.1% of them who died at home with the cause of death not determined by medical personnel. This result mirrored that of Malaysian Dialysis and Transplant Registry (MDTR) data on causes of mortality among ESRD patients, except that CV deaths ranked first in MDTR, followed by Sepsis, and Died at Home<sup>16</sup>. Sepsis in ESRD population carries a 50-fold higher risk of mortality compared to the general population<sup>17</sup>. A single-centre study found a 25.6% mortality rate at 28 days after discharge from hospital for an admission of sepsis among ESRD patients<sup>18</sup>. In addition to high mortality rate, the standard protocol for management of sepsis has its limitations in ESRD populations and has to be applied cautiously<sup>19</sup>, making the management of sepsis in this group of population challenging. The probable explanation for Infection and Sepsis as the number one cause of death in our studied population was that ESRD patients are less immunocompetent and prone to infection and sepsis after hospital admissions. Exposure to pathogens in hospitals and dialysis centres, dialyser reuse, dialysis catheter use, invasive procedures in hospitals, requirement of central venous cannulation during hospital stay, underlying diabetes, age factor, and deterioration of nutritional status after hospital admission are the other probable explanations<sup>20,21,22</sup>. The mortality data in our study highlighted the need to look into factors in minimising infection risks in ESRD population, and in another way emphasises the importance of strict adherence to infection control strategies.

## Conclusion

Our study found that fluid overload, vascular access related issues, respiratory tract infections and coronary events are the commonest reasons of admissions among ESRD patients receiving maintenance RRT. Rate of readmission is high at almost one in every two patients within 90 days of discharge. Vascular access related issues tends to be unsolved and becomes the commonest reason of readmission at 90 days.

Rate of mortality within 90 days of admission to hospital among this group of population is high at almost 18%. Common causes of death within 90 days of discharge are Infection and Sepsis, ACS, and "Died at Home". The results of this single centre study has its limitations if we generalise the data in Malaysia. Nevertheless, certain results on admissions, readmissions, and mortality prompt future larger research in this country to look into the problems faced, as they carry significance not only on patients' outcome, but also on health care cost and resources.

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