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# SURVIVAL OF PATIENTS WITH END-STAGE KIDNEY DISEASE UNDERGOING HAEMODIALYSIS IN BRUNEI DARUSSALAM.

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## ABSTRACT

**Background:** Haemodialysis is the main modality of kidney replacement therapy in Brunei, accounting for more than 85% of all end stage kidney disease (ESKD) patients in the country. This study aims to evaluate the survival and factors associated with poor outcomes in incident ESKD patients undergoing haemodialysis in Brunei. **Methodology**: Data from all incident ESKD patients from 2018 to 2020 in Brunei were extracted from the Brunei Dialysis and Transplant Registry. Kaplan-Meier survival curves and Log-Rank test were performed for statistical significance. **Results**: 410 patients satisfied the inclusion/exclusion criteria and were included for statistical analysis. The total follow-up period for the 410 patients was 1167 months. Kaplan-Meier survival plots showed an overall actuarial patient survival of 93%, 86%, 74% and 64% at 6, 12, 18 and 24 months. Diabetic patients, with a survival of 93%, 84%, 71% and 59%, were significantly inferior to patients with other kidney diseases (95%, 92%, 83% and 81%) on Log Rank test at the same 6 monthly reference timepoints. Older patients and those of Chinese ethnicity have significantly lower survival. **Conclusion**: Haemodialysis patients in Brunei have a comparable 1-year survival with other countries, but slightly inferior survival beyond that. Comparing results from previous national studies, HD patients have inferior outcomes as opposed to PD and transplant patients. This study gives supporting evidence for the promotion of PD and transplant as the preferred modalities for ESKD patients in the country.

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# SURVIVAL OF PATIENTS WITH END-STAGE KIDNEY DISEASE UNDERGOING HAEMODIALYSIS IN BRUNEI DARUSSALAM.

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## ABSTRACT

**Background:** Haemodialysis is the main modality of kidney replacement therapy in Brunei, accounting for more than 85% of all end stage kidney disease (ESKD) patients in the country. This study aims to evaluate the survival and factors associated with poor outcomes in incident ESKD patients undergoing haemodialysis in Brunei. **Methodology**: Data from all incident ESKD patients from 2018 to 2020 in Brunei were extracted from the Brunei Dialysis and Transplant Registry. Kaplan-Meier survival curves and Log-Rank test were performed for statistical significance. **Results**: 410 patients satisfied the inclusion/exclusion criteria and were included for statistical analysis. The total follow-up period for the 410 patients was 1167 months. Kaplan-Meier survival plots showed an overall actuarial patient survival of 93%, 86%, 74% and 64% at 6, 12, 18 and 24 months. Diabetic patients, with a survival of 93%, 84%, 71% and 59%, were significantly inferior to patients with other kidney diseases (95%, 92%, 83% and 81%) on Log Rank test at the same 6 monthly reference timepoints. Older patients and those of Chinese ethnicity have significantly lower survival. **Conclusion**: Haemodialysis patients in Brunei have a comparable 1-year survival with other countries, but slightly inferior survival beyond that. Comparing results from previous national studies, HD patients have inferior outcomes as opposed to PD and transplant patients. This study gives supporting evidence for the promotion of PD and transplant as the preferred modalities for ESKD patients in the country.

**Keywords: Brunei, End Stage Kidney Disease, Haemodialysis, Kidney Replacement Therapy, Survival.**

## INTRODUCTION

Haemodialysis (HD) is the most commonly utilised Kidney Replacement Therapy (KRT) in Brunei Darussalam, accounting for 85% of treatment for End Stage Kidney Disease (ESKD) patients.[1] Brunei has one of the highest prevalence and incidence of ESKD in the world with rates of 1944 and 479 per million population (pmp) respectively in 2020.[1] This translated to 881 dialysis patients at the end of 2020 and 217 new patients for the entire year.[1] After accounting for deaths, there was a net increase of 95 prevalent patients (209 pmp) from the previous year. The ten-year trend (2011-2020) for annual increment in prevalent and incident numbers were 42.2 and 9.9 pmp per year[1]; with 2020 demonstrating an uncharacteristic hike in numbers, incongruent with the previous trends.

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ESKD patients have a worse overall survival compared to the general population.[2] Amongst patients on KRT, kidney transplant patients have the best survival record[3], whilst many studies have shown that peritoneal dialysis patients have an equivalent or superior survival to haemodialysis in the first few years of therapy.[4–6] Cardiovascular disease and infections are the two major causes of deaths worldwide[2,7]and this pattern is also observed in the local population in the last ten years.[1]

There are many factors that can influence the survival outcome of haemodialysis patients. Amongst the non-modifiable factors are age, race, country, comorbid conditions, underlying aetiological disease, psychosocial factors and residual renal function.[8–14] Modifiable risk factors include nutrition, haemoglobin level, treatment compliance, physical activity, dialysis adequacy, dialysis access and pre-dialysis care.[15–22] A local study on pre-dialysis care showed that patients who were prepared and educated in pre-dialysis clinics were associated with a 34% decreased risk of dying, despite having more diabetes and being older.[22]

This study aims to evaluate patient survival in incident HD patients in Brunei between 2018-2020, and factors that are associated with poor outcomes.

## METHODOLOGY

This is a retrospective Registry cohort study of all incident ESKD patients in Brunei for a period of 3 years. The inclusion criteria included all incident patients who started HD from 1st January 2018 to 31st December 2020 in the country and who had HD for longer than 3 months. Patients who underwent HD for acute kidney injury, for less than 3 months, or died within 3 months of starting HD or were lost to follow-up were excluded from the study. This study was carried out as part of the Department of Renal Medicine's Key Performance Indicators Audit project to highlight areas for service improvement and to assess the outcome of patients on HD.

All necessary data from the study population were extracted from the Brunei Dialysis and Transplant Registry (BDTR). Demographic data included gender, race, aetiology, age at start of dialysis and date of start of dialysis. All baseline demographic characteristics were determined at the start of HD initiation. Dates of exit from HD program such as transfer to PD, transplant or loss to follow up were also recorded and patients were recorded as still alive at this time point and censored off during survival analysis. Survival of patients who exited the HD program for alternative KRT were easily confirmed as all patients undergoing KRT were entered into the Brunei Dialysis and Transplant Registry except those who were lost to follow. Survival status for this group were cross referenced by searching for the patients known status in Bru-HIMS database, which is the Brunei Health Information Management system, an electronic patient management database for the whole country.

Primary outcome for the study was defined as death from all causes whilst secondary end-points were 'transfer to PD' and 'kidney transplantation'. Patients achieving secondary endpoints were excluded from the final survival analysis to ensure the results obtained was based purely on a sample of HD patients and not influenced by the better survival of kidney transplant patients or patients on PD.

Statistical analysis was performed with Statistical Package for the Social Sciences software (version 18.0; SPSS Inc, Chicago, IL, USA). All data were expressed using measures of central tendency and dispersion (means and standard deviations) for quanti-

tative variables. For ease of survival analysis, variables were categorised into groups: gender (male and female), age at onset of HD (less than 40, 40-59, 60-79, greater than 80 years), aetiology of ESKD (Diabetes Mellitus and others) and ethnicity (Malay, Chinese, others). Continuous data (parametric data) were analysed using Student T test for two groups and One-way ANOVA for multiple groups with Scheffe's procedure for post hoc analysis. Survival analysis was performed using Kaplan-Meier method and log-rank (Mantel-Cox) test to compare the curves based on variables of interest. Results were considered statistically significant if the p-value was less than 0.05.

## RESULTS

A total of 538 ESKD patients were registered on BDTR as undergoing KRT during the 3 years study period. One hundred and fifteen patients were excluded for failing to meet the study inclusion and exclusion criteria (Figure 1). Of the 423 eligible patients, a further 13 were excluded for reaching secondary end points. Hence only 410 patients were eligible and included for the final analysis with a total follow-up period of 1167 months. Infection (29%) and cardiovascular disease (21%) were the two most common causes of deaths in the cohort. Table I shows the basic demographics of the 410 incident HD patients included in the study. Majority (49%) were in older middle age groups, ranging from 40-59 years of age. Thirty-eight percent were above the age of 60 years. Ratio of male:female patients on HD was 1.19:1. Majority (86%) were Malay, 8% were Chinese and the remaining 6% were of other ethnic origins. The most common aetiology of ESKD was diabetes mellitus in 78.3% of cases. Proportion of patients starting on HD were about the same for each year.

Kaplan-Meier survival plots showed an overall actuarial patient survival of 93%, 86%, 74% and 64% at 6, 12, 18 and 24 months. Diabetic patients, with a survival of 93%, 84%, 71% and 59%, were significantly inferior to patients with other kidney diseases (95%, 92%, 83% and 81%) on Log Rank test at the same 6 monthly reference time points (Table II: $p<0.05$). There was also a significant survival advantage in patients of Malay and other ethnicity compared to patients of Chinese ethnicity (Table II: $p<0.05$). Younger age groups have higher survival probabilities over older age groups, but there was no significant gender difference (Table II: $p<0.05$). Figures 2a-e represent the Kaplan-Meier Survival curves for the different categories.

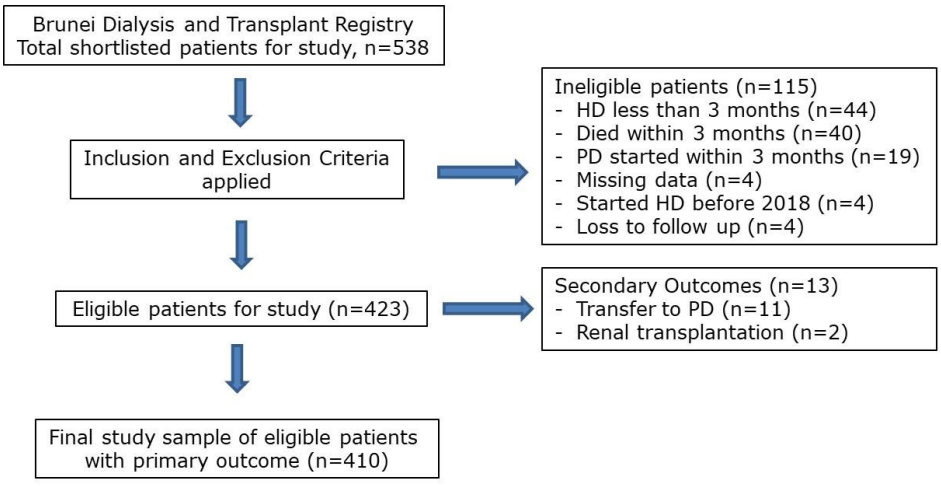


**Figure 1: Flowchart depicting the eligibility for HD survival analysis.**

**Table I: Demographics of incident HD patients (2018-2020).**

| Demographic variables | Frequency n (%) |
|---|---|
| **Total** | 410 (100%) |
| **Age Groups** | |
| < 40 years | 56 (14) |
| 40-59 years | 199 (49) |
| 60-79 years | 147 (36) |
| > = 80 years | 8 (2) |
| **Gender** | |
| Male | 223 (54) |
| Female | 187 (46) |
| **Race** | |
| Malay | 351 (86) |
| Chinese | 33 (8) |
| Others | |
| **Aetiology of ESKD** | |
| Diabetes Mellitus | 321 (78) |
| Others | 89 (12) |
| **Year of initiating HD** | |
| 2018 | 95 (23) |
| 2019 | 154 (38) |
| 2020 | 161 (39) |

## DISCUSSION

The 1- and 2- year survival of HD patients in Brunei were 86% and 64% respectively. Comparatively, these results were similar to results from HD patients in Singapore (1 and 3 year survival of 91% and 61%) and Malaysia (1 and 3 year survival of 88% and 68%).[23,24] Projected 3-year survival data through extension of the Kaplan-Meier analysis show a likely actuarial survival of 57%, which is poorer compared to most countries. The Dialysis Outcomes and Practice Patterns Study (DOPPS) showed a 1 year crude survival rate of 93%, 84% and 78% in Japan, Europe and USA respectively.[11] Australia and New Zealand reported similar first year survival (87% and 90% respectively) but superior survival at three years (68% and 71% respectively).[25] Variability in demographic, healthcare access, comorbid conditions and transplant availability explained part of the variances in mortality between countries.[26]

Comparing survival of HD patients to those who underwent PD or renal transplantation in Brunei, the latter two groups showed better patient survival. PD survival at 1,3 and 5 years were 91%, 73% and 56% respectively in Brunei[1], which were marginally superior to Singapore, Malaysia, Australia and New Zealand.[23-25] Transplant survival in Brunei at

**Table II: Analysis of haemodialysis patients' demographic, ethnicity and aetiology of ESKD with survival at 6, 12, 18 and 24 months.**

| Variables | Kaplan-Meier survival Percentage | | | | P value |
|---|---|---|---|---|---|
| | 6 months (%) | 12 months (%) | 18 months (%) | 24 months (%) | |
| **Total Sample (n)** | 93 | 86 | 74 | 64 | |
| **Age group** | | | | | |
| <40 | NA | 88 | 84 | 77 | ***<0.05**** |
| 40-59 | 95 | 89 | 78 | 70 | |
| 60-79 | 90 | 82 | 64 | 50 | |
| >80 | NA | 74 | NA | 51 | |
| **Gender** | | | | | |
| Male | 94 | 88 | 75 | 63 | 0.515 |
| Female | 92 | 84 | 71 | 62 | |
| **Racial Ethnicity** | | | | | |
| Malay | 94 | 86 | 75 | 65 | ***<0.05**** |
| Chinese | 85 | 80 | 71 | 35 | |
| Others | NA | 94 | 81 | NA | |
| **Aetiology of ESKD** | | | | | |
| DM | 93 | 84 | 71 | 59 | ***<0.05**** |
| Others | 95 | 92 | 83 | 81 | |

***Statistical significance based on Log-Rank Mantel-Cox test.

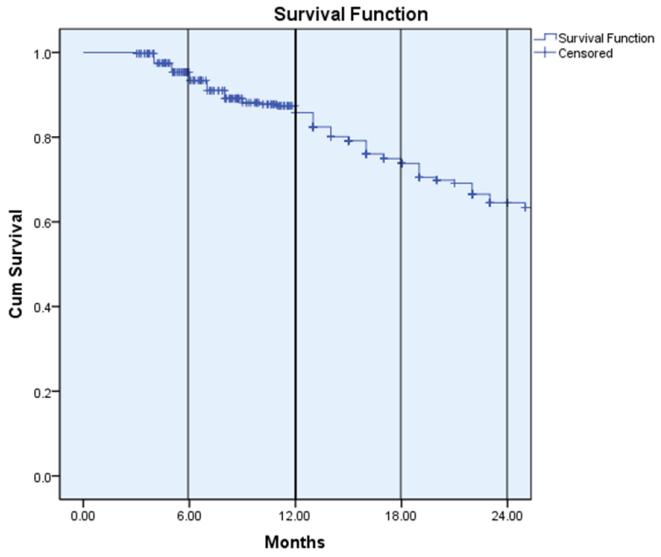


**Figure 2a: Kaplan-Meier Survival curve for incident HD patients (2018-2020).**

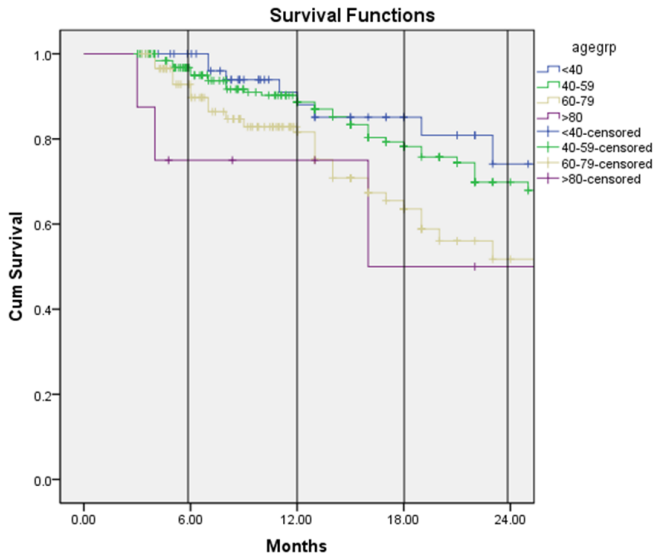


**Figure 2a: Comparison of Kaplan-Meier survival curves between age groups in incident HD patients (2018-2020), showing statistically significant difference in survival between the groups (*p<0.05)*.**

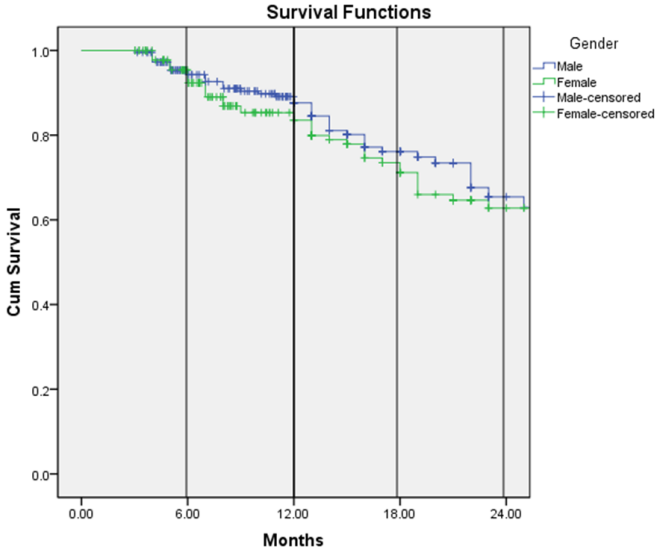


**Figure 2b: Comparison of Kaplan-Meier survival curves between gender in incident HD patients (2018-2020), showing no statistical significant difference in survival (*p<0.05*).**

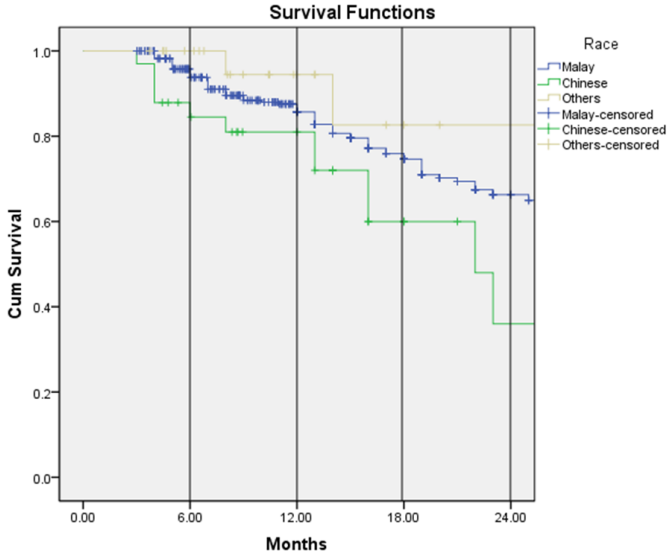


**Figure 2c: Comparison of Kaplan-Meier survival curves between ethnicity in incident HD patients (2018-2020), showing statistically significant difference in survival (*p<0.05)*.**

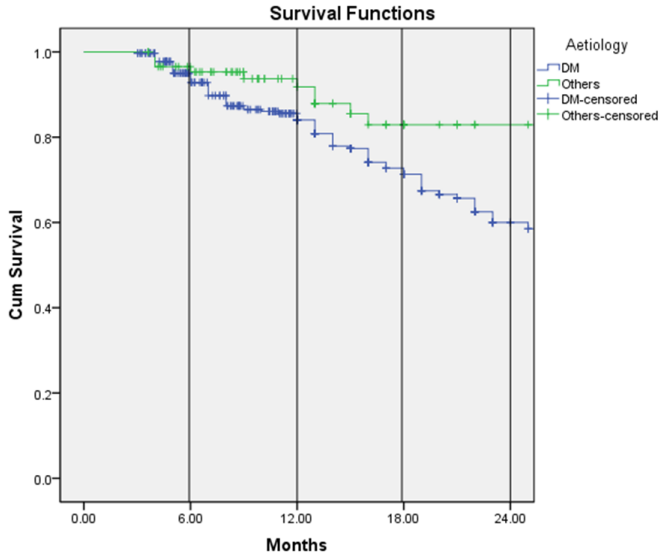


**Figure 2e: Comparison of Kaplan-Meier survival curves between incident HD patients with and without DM (2018-2020), showing statistically significant difference in survival (*p<0.05)*.**

**DM=Diabetes Mellitus**

5 and 10 years were 93% and 90%, on par or better than most developed countries.[27] It is possible that PD and transplant patients had better outcomes than HD because their patients were younger and have less comorbidities, although data were not collected to substantiate this assumptions.

Diabetes, old age and patients of Chinese origin have significantly poorer survival outcomes. Not surprisingly, most studies have shown that diabetes patients have more complications on dialysis due to inherent risks derived from the disease: cardiovascular, peripheral vascular, cerebrovascular and infection risks.[28-29] Van Diepen et al defined a prediction model with seven factors that predicts mortality at one year: age, smoking, macrovascular complications, duration of diabetes, Karnofsky scale, serum albumin and haemoglobin level.[30] Age at start of dialysis has negative connotation to outcome, but more importantly, functional impairment, cognitive impairment and history of falls were significantly and independently associated with increased mortality in elderly haemodialysis patients.[31] The Singapore Renal Registry reported a similar survival between Malays

and Chinese HD patients at 1,5 and 10 years (90%, 63% and 38% vs 91%, 61% and 36% respectively).[23] The reported survival inferiority amongst Chinese also extended to the PD population in Brunei, where Malay and Chinese patients had a mean survival time of 31.70 ± 22.76 and 23.82 ± 18.16 months respectively in a ten-year follow up study.[1]

The focus to improve HD survival should be on improving modifiable risk factors described previously: nutrition, treatment compliance, physical activity, dialysis adequacy, dialysis access and pre-dialysis care. We hope to intensify dietary input from doctors, dieticians and healthcare workers to shore up dietary compliance with phosphorous, potassium and salt; and to improve intake of good quality protein, in line with the National Kidney Foundation Clinical Practice Guideline Dialysis Outcomes Quality Initiative (KDOQI) target of 1.2g/kg/day.[32] Non-compliance with medication and treatment often lead to wastage of resources, but more seriously, it results in suboptimal dialysis and inadequate correction of biochemical parameters which can increase morbidity and mortality.[33] Increasing habitual physical activity can improve overall and cardiovascular fitness, even amongst patients on maintenance HD, was associated with reduced mortality.[34] Dialysis adequacy through improving dialysis blood flow rates and usage of high flux dialyser can facilitate the clearance of metabolic toxins and improve survival.[35] Pre-dialysis care through timely creation of arteriovenous fistula and psychosocial preparation has a significant impact not only on survival, but quality of life.[22]

We acknowledged that there were some limitations to this study. The information utilized in this study was secondary data extracted from the BDTR, hence we were not in complete control of the data being collected. Ideally, we would have liked to collect data for co-morbidities (particularly ischaemic heart and cerebrovascular disease), vascular access, compliance with treatment and medication and psychosocial history. The additional information would have added depth to the analysis and enabled a more accurate regression analysis to ascertain the impact of individual factors on survival.

## CONCLUSION

This study shows that HD patients in Brunei have a comparable 1- survival with other countries, but projected survival was inferior beyond 2 years. Compared to PD, HD survival was also inferior but this could be related to the unequal demographics in both groups. A multitude of factors have been implicated in HD survival, but non-modifiable factors like disease aetiology, age and race played a significant role in our cohort. More efforts are needed to address modifiable factors like dialysis adequacy, vascular access and treatment compliance. The poor HD survival, relative to other KRT modalities, provides evidence to champion and drive a national PD and transplant preference policy for ESKD patients in Brunei in the future.

## CONFLICTS OF INTEREST

There are no conflicts of interest among authors in this study.

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