Othman et al.
Brunei International Medical Journal
2025;21:34-41

Brunei International Medical Journal

Original Article Open Access

Peritoneal Dialysis in Brunei Darussalam: A Historical Review and Survival Analysis (1993-2020)

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Abstract

Introduction: Brunei Darussalam started a peritoneal dialysis (PD) programme in 1993. However, the number of PD patients have stagnated in the last few years, despite the advent of a PD-preference policy in 2014 with retention of patients on the programme being one of the main goals. The main objective of this retrospective observational national study was to assess overall, patient and technique survival in all patients who started PD in the country since the inception of the programme, along with factors that may influence survivals. **Methods and Methods:** Data were collected from historical archives from the Ministry of Health and the Brunei Dialysis and Transplant Registry. Analysis of survivals were done through Kaplan-Meier survival plots and log rank tests. Multivariate Cox analysis was used to determine factors that affect survivals. **Results**: This study recruited 403 out of 463 eligible patients, with a mean age of 48.20 ± 16.48 years. Diabetes mellitus, continuous ambulatory peritoneal dialysis and male patients accounted for 48%, 58% and 52% of the cohort respectively. The overall actuarial survival at 1,3,5 and 10 years were 81%, 51%, 29% and 13% respectively. Patient and technique survivals for the same timepoints were 89%, 69%, 49% and 31%; and 90%, 72%, 60% and 44% respectively. Absence of diabetes mellitus and younger age of starting PD were identified as significant independent variables for retention in the PD programme. **Conclusions:** This study showed that PD patients Brunei Darussalam has comparable mean survival rates with published data in the international literature and absence of diabetes mellitus and younger age at starting PD are significant predictors of retention in the PD programme.

Keywords: Peritoneal dialysis; Chronic kidney disease; Renal replacement therapy; Survival

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INTRODUCTION

Brunei Darussalam, a small country in South East Asia, has one of the highest prevalence and incidence of end stage kidney failure (ESKF) in the world.[1] The Brunei Dialysis and Transplant Registry (BDTR) recorded an ESKF prevalence and incidence of 1708 and 382 per million population (pmp) respectively in 2019, which would have placed the country within the world's top ten on the United States Renal Data System (USRDS).[2,3] Brunei Darussalam provides universal healthcare coverage to all its citizens and permanent residents, with free dialysis treatment, hospitalisation and medications. Peritoneal Dialysis (PD) accounted for 10% of all patients on kidney replacement therapy (KRT) in 2019.[2] PD, in the form of hospital-based intermittent peritoneal dialysis (IPD), has been periodically used since the 1960s for patients with acute kidney injury, but a definitive continuous ambulatory peritoneal dialysis (CAPD) programme was only formally introduced in 1993.[4] Progressively, through targeted and focused campaigns espousing the benefits of home-based dialysis treatment and patient's autonomy, more patients were recruited into the programme resulting in a peak KRT penetration in the early 2000s. However, its popularity began to wane in the late 2000s due to long waiting time for PD tube insertions and perceived poor survival amongst patients. Automated peritoneal dialysis (APD) was introduced in 2008 to enhance flexibility and convenience of the treatment, but unfortunately, it also failed to invigorate real interest.[5] A government-endorsed PD-preference policy was implemented in 2014 to prioritise PD usage over haemodialysis (HD) through preferential counselling, restructuring of framework and educational initiatives.[6] The strategy boosted the numbers of PD patients between 2014 and 2018, with a 76% increment within 4 years.[7] Regrettably, the prevalence appeared to have plateaued again in the past few years, but refreshening and remodeling of the PD-preference policy is afoot to rejuvenate and spruce up the programme.[8] One of the main priorities is to obtain baseline survival data and to facilitate retention of patients onto the programme by improving patient and technique survival

There are limited national studies reporting on the survival of PD patients; particularly in smaller or developing countries, which usually lack reliable national registry data. This national study provides a comprehensive analysis of PD survival, incorporating all patients who joined the programme since its inception in 1993. The primary outcome of this retrospective observational cohort study was to assess the overall, patient and technique survival of peritoneal dialysis patients in the country. The secondary outcomes were to analyse factors that may influence survival, benchmark national survival rates against other countries, chart chronologic national prevalence, incidence and penetration of PD; and document demographic data of all current and historical PD patients.

MATERIALS AND METHODS

Study population; All incident PD patients in Brunei were identified from the archives of the Department of Renal Services, Ministry of Health and the Brunei Dialysis and Transplant Registry (BDTR). The inclusion criteria included all incident patients who started PD from 1st January 1993 to 31st December 2020. The exclusion criteria were patients that were dialysed for acute kidney injury and who were on peritoneal dialysis for less than 3 months. Altogether, 463 patients were included in the shortlist, of which 60 were deemed ineligible because of AKI (n=11) and being on PD for less than 3 months (n=49). Patients who were on PD for less than 3 months included deaths (n=25), prevalent patients (n=10), changed minds and transfer to HD (n=6), technical failure and transfer to HD (n=6) and unknown reasons (n=2).

Data collection: Data from all incident PD patients in Brunei were extracted from the archives of the Department of Renal Services, Ministry of Health and the BDTR. Demographic data included gender, race, aetiology, type of PD, age at start of dialysis and date of start of dialysis. All baseline demographic characteristics were determined at the start of PD initiation. Dates of

exit from PD programme (transfer to HD, death, transplant and loss to follow up) were also recorded for survival analysis. Actuarial survival was defined as survival at predetermined intervals of 1,3,5 and 10 years. Overall survival was defined as patients remaining in the PD programme after drop-outs from deaths and technique failure. Technique failure was defined as transfer to HD from all causes including ultrafiltration failure, mechanical problems, patient dissatisfaction, peritonitis, catheter-related problems and insufficient dialysis; whilst patient survival was defined as being alive at the actuarial defined intervals (1,3,5 and 10 years). For survival analyses, variables were categorised into groups; gender (male and female), age at onset of PD (less than 20, 21-40, 41-60, greater than 60 years), aetiology of ESKF (diabetes mellitus, glomerulonephritis and others), types of PD (CAPD and APD) decade of PD start (1990s, 2000s, 2010s) and race (Malay, Chinese, others).

Statistics: Statistical analysis was performed with the 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 quantitative variables. Kaplan-Meier method was used for overall, technique and patient survival and log-rank (Mantel-Cox) test to compare the curves. Risk factors predictive of outcomes were presented for multivariate Cox analysis, with application of backward stepwise elimination procedure to determine significance. Results were considered statistically significant if the p-value was less than 0.05. In patient survival analysis; patients were censored if they were lost to follow-up, who received kidney transplants or transferred to HD. In technique survival analysis; patients who died, lost to follow-up and received kidney transplant were censored. For overall survival analysis, only patients who transferred to HD and died were included as outcome.

RESULTS

Incidence and prevalence

Figure 1 shows the trend of incidence, prevalence and penetration of PD over a 28-year period since the inception of the programme in 1993. Peak PD numbers were recorded in 2018 (N=82), a few years after the introduction of the PD preference policy, as reflected by a 76% increase in PD numbers since 2013. Peak penetration for PD was reported in 2004, when 18% of all KRT patients were on PD. The introduction of APD in 2008 did not make a significant impact on prevalence and incidence.

Patients' characteristics are described in Table I. The mean and median age for starting PD was 48.20 ± 16.48 and 49 years respectively. There was a 52% male preponderance. 84% of patients were from ethnic Malay origin, whilst 12% were from Chinese origin. PD was started in the 1990s, 2000s and 2010s in 13%, 45% and 43% respectively. The aetiology of ESKF were diabetes mellitus (48%), glomerulonephritis (24%) and others (28%). There were 171 (42%) APD and 232 (58%) CAPD patients. Age groups of patients were <

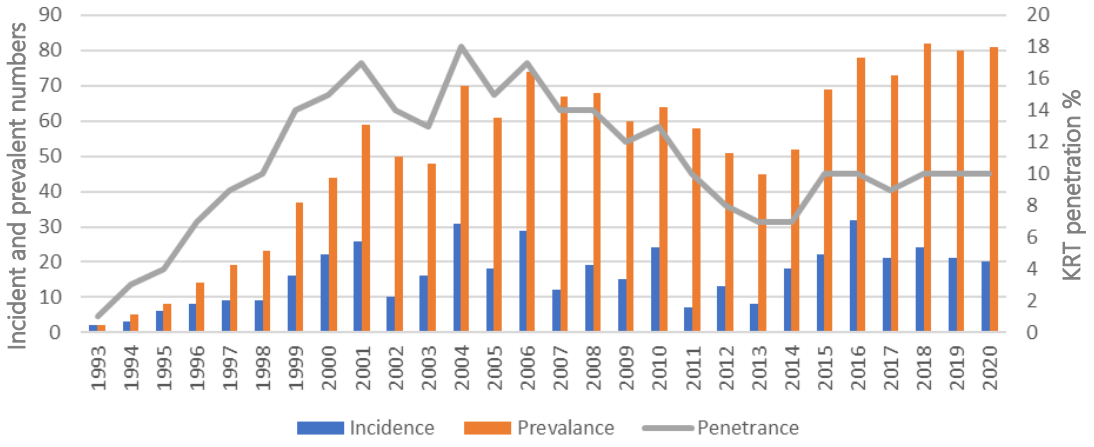

Figure 1: The national incidence, prevalence and KRT penetration of PD in Brunei (1993-2020).

Table I: Demographics and characteristics of PD patients (N=403).

Variables		N (%)
Age group	< 20 years	29 (7)
	21-40 years	84 (21)
	41-60 years	195 (48)
	> 60 years	95 (24)
Gender	Male	210 (52)
	Female	193 (48)
Race	Malay	338 (84)
	Chinese	49 (12)
	Others	16 (4)
Decades	1990s	51 (13)
	2000s	172 (43)
	2010s	180 (45)
Aetiology	Diabetes Mellitus	194 (48)
	Glomerulonephritis	95 (24)
Types of PD	APD	171 (42)
	CAPD	232 (58)

PD: Peritoneal dialysis, APD: Automated peritoneal dialysis: CAPD Continuous abdominal peritoneal dialysis

Survival analyses

403 patients were included in the demographic and survival analysis. The recorded outcomes were deaths (n=179), transfer to HD or technique failure (n=138), transplant (n=15) and migrate to other country (n=1). At the end of the study on 31st December 2020, there were 70 prevalent patients without an exit outcome.

Overall actuarial survival (Figure 2a) of patients in the PD programme was 81%, 51%, 29% and 13% at 1,3,5 and 10 years.

Patient survival was 89%, 69%, 49% and 31% (Figure 2b) and technique survival (Figure 2c) was 90%, 72%, 60% and 44% for the same time periods.

Log rank test (Mantel-Cox) revealed a significant difference in survival between patients with diabetes mellitus (75%, 38%, 17%, 0%), glomerulonephritis (89%, 76%, 53%, 27%) and other causes of kidney diseases (81%, 48%, 29%, 18%) [log rank 46.98, P<0.05].

Younger age at start of PD also had a significant impact on survival, with superior survival reported in the 21-40 years age group (91%, 66%, 39%, 26%) and inferior survival in the > 61 age group (75%, 33%, 10%, 0%) [log rank 37.45, P<0.05]. Unlike the analysis of mean months on PD, there was no significant association in survival between the types of PD (log rank 0.22, P=0.65) and decades of PD start (log rank 3.04,

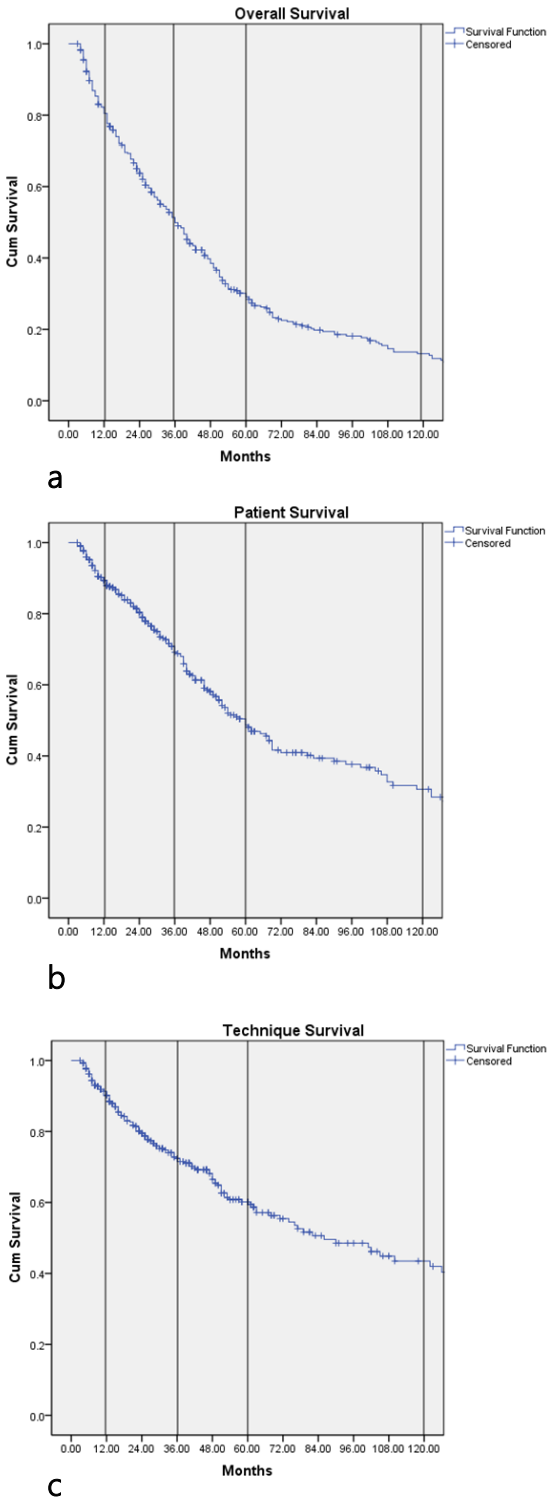

Figure 2: a) Kaplan Meier graph for overall survival, b) Kaplan Meier graph for patient survival, and c) Kaplan Meier graph for technique survival.

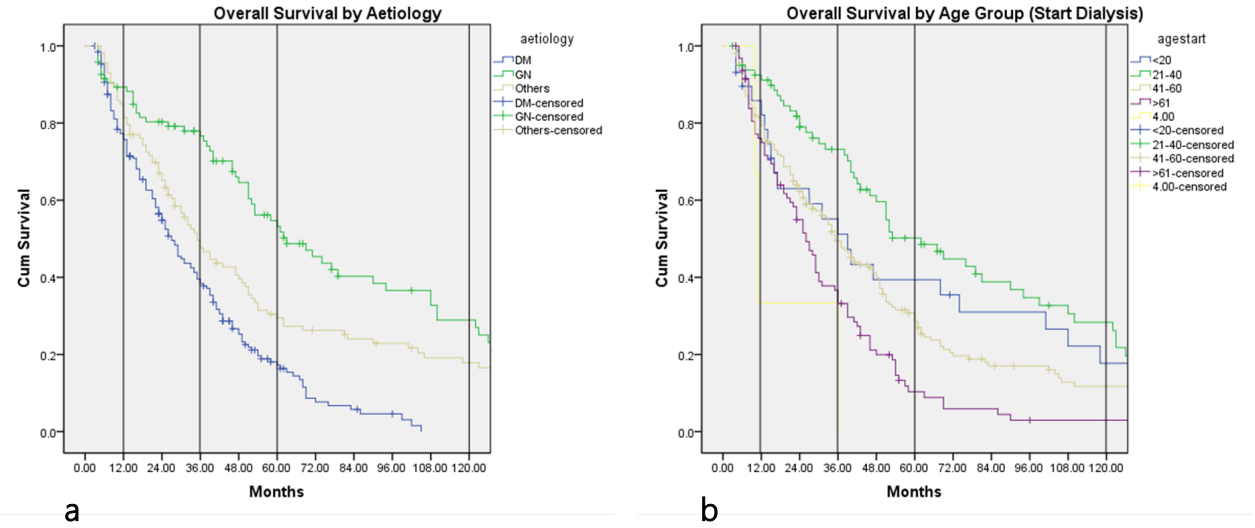

Figure 3: a) Kaplan Meier graph for overall survival by aetiology which shows GN has better outcome compared to 'Others' and DM, and b) Kaplan Meier graph for overall survival by age group (upon starting dialysis).

P=0.22). Multivariate Cox proportional hazards modelling confirmed that diabetes mellitus (and age of start (p<0.05) were independent predictors of overall survival, whilst gender (p=0.813), race (p=0.339), PD type (p=0.982) and decade of start (p=0.882) were not significant predictors.

DISCUSSION

Akin to the trend in most countries, the prevalence and incidence of ESKF in Brunei Darussalam are increasing. Even with its potential socio-economic and lifestyle perquisites, PD has struggled to keep pace with HD in the country. This lackluster trend is consistently reported in most countries in the world, although countries who purported to have PD-favouring policies have experienced positive growth.[9] The introduction of the PD-preference policy has reinvigorated interest in 2014, but efforts to sustain PD growth were hampered by the relative lack of trained professionals, long waiting list for PD tube insertions and poor public perception of this modality in the country.[6] On-going PD policy changes focused on improving education amongst stakeholders (patients, carers, nurses and doctors), increasing competition for PD providers to reduce cost, reducing waiting list for PD surgery and retaining patients on the programme, through mitigation of complications and prevention of deaths.[8] Although there is no major difference between costing of HD and PD in the country, the policy aims to increase PD penetration in the population on the basis of quality of life improvement and human resources limitations. [6-7]

Our actuarial patient survivals of 89%, 69%, 49% and 31% and technique survivals of 90%, 72%, 60% and 44% at 1,3,5 and 10 years were comparable with many countries. (Provide references- will be similar to the To make sense out of the results, we compared and summarized results according to regions: South East Asia (SEA), East Asia, Australasia, Europe, America and Africa (Table II). Like-for-like comparisons were difficult because of different criteria and methodologies used to define survivals. Most studies, including our study, included survival data after 3 months on PD. [10-17] But others did not specify precise definition of this criterion in their published write-up [18-22]. Regionally, our results were comparable to those from Singapore, Thailand and Malaysia, likely stemming from similar racial-ethnic demographics and, in spite of financial-economic differences.[18-20] Many large studies had established a few norms in PD survival data. Patients with diabetes mellitus, advanced age, co-morbidities, on CAPD and from older historical cohorts tended to have inferior outcomes.[22-24] Additionally, other studies have reported that other less studied factors like residual glomerular filtration rate, systolic blood pressure, dialysis clearance, high PET type and serum albumin were independent risk factors for survival.[25] Our study showed that

Table II: International comparison of survival rates to the current study.

Author (year)	Region	Country	Sample size	Mean age	DM (%)	Patient Survival (%)					Technique Survival (%)				
						1 year	2 years	3 years	5 years	10 years	1 year	2 years	3 years	5 years	10 years
Othman et al Current	South East Asia	Brunei Darussalam	403	48	48	89	80	69	49	31	90	80	72	60	44
Choo et al (2012) [18]		Singapore	1015	58	58	89	78		40	15	93	85	-	65	33
Changsirikulcha et al (2018) [19]		Thailand	11813	54	61	83	-	64	54		95	-	88	81	-
Malaysian Renal Registry (2018) [20]		Malaysia	11021	57***	65***	87	-	61	44	24	78	-	46	26	5
Xi et al (2018) [10]	Asia	China	533	48	24	93	-	81	64	36	98	-	93	85	62
Huang et al (2020) [12]		Taiwan	2809	-	27	90	-	68	56	35	-	-	-	-	-
Ho et al (2013) [11]		Hong Kong	3573	62	46	91	-	70	51	27	-	-	-	-	-
Lee et al (2016) [15]		South Korea	7614	55-58****	54-50****	90	81	74	-	-	95	90	84	-	-
Nadeau-Fredette et al (2015) [13]	Oceania	Australia / New Zealand	10710	62	35	89	76	-	44	-	-	-	-	-	-
Nadeau-Fredette et al (2020) [14]	America	Canada	15469	63	39	92	81	-	50	-	-	-	-	-	-
Guo et al (2003) [21]		USA	11137	53-55****	43-45****	82	69	58	-	-	-	-	-	-	-
Mujais et al (2006) [22]		USA	40869	53-54****	43-45****	86	76	66	-	-	81*/ 74**	67*/ 60**	56*/ 50**	-	-
EDTA-ERA (2018) [17]	Europe		4085	63***	20***	87	-	63	44	-	-	-	-	-	-

DM: Diabetes Mellitus
* patients new to dialysis
** patients transferred from HD
*** For entire KRT population (Mean age and % DM were not specifically mentioned in registry)
**** Mean age and % DM presented in stratified groups
***** Median age

absence of diabetes mellitus and younger age at starting PD were the most important determinants of survival.

Moving forward, this study has allowed us to scrutinise and introspect our service to examine for possible factors that can be addressed which may improve technique survival. Although not entirely representative of the study cohort, a recent unpublished study from the University of Brunei Darussalam involving 126 PD patients, identified 37 patients who transferred to HD between 2009 and 2018.[26] The main reasons for HD transfer were peritonitis (n=18), patient dissatisfaction (n=6), and poor solute and fluid clearance (n=5); which emphasized the importance of optimising peritonitis prevention and treatment, and adequacy management and assuaging patients' social burden to improve retention on the programme. Peritonitis rates in the country in the last decade had consistently been above the recommended target by ISPD (1 episode every 24 months or 0.5 episodes per patient year at risk), with the latest 2019 rate being 1 episode every 53 months or 0.22 episodes per patient year.[2] However, there was a trend towards culture-negative peritonitis in the previous few years, which led to recent initiatives to engage with the Department of Microbiology to improve sample collection and culture methods, and to map out microbial sensitivities for the population.[2] A previous study in Brunei Darussalam reported that the majority of the population had a high (18%) or high average (56%) transporter status (defined as permeability of peritoneal membrane to facilitate fluid and solute transfer), which was usually associated with impaired ultrafiltration, fluid overload and technique failure.[27-29] Going by the prevailing transporter status of the prevalent population and evidence for membrane preservation, momentum has been buoyed by the PD preference policy to embrace wholesale usage of physiologic solution in the country.[30] Lastly, patient dissatisfaction stemming from lack of perceived social support at home, poor confidence in therapy and poor support by healthcare professionals will be addressed by intensification and periodic augmentation of training through regular seminars, workshops and social events to improve patients' rapport and relationship with staff.

The annual death rate for the local PD population has hovered between 3-13% in the last five years.[2] The chief causes of death for PD patients in the aforementioned university study [27] between 2009 and 2018 were infections (56%) and cardiovascular diseases (24%), similar to the pattern and trend observed in the entire KRT cohort in the country.[2] The BDTR in 2021 reported similar causes of deaths with infections (38%) and cardiovascular diseases (23%) as the two main causes. A previous study in Brunei looking at incident HD patients between 2018 and 2020 showed an overall actuarial patient survival of 86% and 64%, at 1 and 2 years respectively, which by comparison is inferior to the rates achieved in the PD population (89%, 69%, 49% and 31% at 1,3,5 and 10 years).

Further scrutiny of BDTR data showed potential suboptimal key performance indicators (KPI) in PD patients that could affect patient survival like mean serum haemoglobin (10.5g/dl), phosphate (1.9 mmol/l), intact PTH (80.9 pmol/l) and dialysis adequacy (weekly kt/v of 1.8). Underperformance of these dialysis parameters; haemoglobin, phosphate, intact PTH and dialysis adequacy, have been consistently implicated in mortality outcomes in PD literature.[32-35] KPIs from our KRT cohort had withstood comparisons with other countries in recent publications, but several changes can still be implemented to improve outcomes.[1-2] Increasing availability and wholesale usage of expensive evidence-based drugs like erythropoietin, calcimimetics and non-calcium-based phosphate binders, along with targeted education to key medical and nursing personnel and adherence to evidence-based guidelines and algorithms can improve the quality of recorded KPIs, and hopefully resulting in better patient survival. Timely referrals and collaborations with cardiologists for screening and interventions could also result in less adverse cardiovascular outcomes.

The retrospective nature of this study meant that there was constraint of data collection that could result in residual confounding and indication bias. We would have liked to collect data for co-morbidities, dialysis vintage, blood KPIs, causes of dropouts, membrane characteristics, solutions usage and psychosocial support (like availability of carers or presence of disability). Fortunately, some data has been recorded in the BDTR to allow interpretations in discussions but the data was not complete enough to be included for the entire research cohort. As such we could not obtain the actual cause of deaths or cause of technical failure in many cases from the earlier cohorts. Given the importance of diabetes mellitus as a predictor of outcome, we would

have liked to authenticate the veracity of our historic data in determining whether diabetes mellitus was an aetiological condition or a coexisting comorbidity. The diagnosis of diabetic nephropathy was mainly established through the presence of diabetes mellitus in the past history, and not through histological diagnosis. Patients under the age of 20 were usually classified as 'paediatric' or 'adolescent' in other survival studies and their inclusion in this 'adult' study may have affected overall outcome.

CONCLUSION

This study has enabled a comprehensive review of the history of PD in the country. It also provides baseline survival data for future comparisons and benchmarking with local and international studies. The survival rates compared favourably to published data on the local HD population, with future endeavors focusing on increasing recruitment and retention of patients on the PD programme.

Abbreviations

PD	Peritoneal dialysis
ESKF	End stage kidney failure
BDTR	Brunei Dialysis and Transplant Registry
KRT	Kidney replacement therapy
IPD	Intermittent peritoneal dialysis
CAPD	Continuous ambulatory peritoneal dialysis
APD	Automated peritoneal dialysis
HD	Haemodialysis
AKI	Acute kidney injury
Pmp	Per million population
USRDS	United States Renal Data System

Ethical Statement

Research ethics statement - Ethics approval was not sought in this study because it was performed as an audit in the Brunei Dialysis and Transplant Registry.

Declarations

All the authors declared no competing interests.

Acknowledgement

None.

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