

ASIA-PACIFIC CHAPTER NEWSLETTER

INTERNATIONAL SOCIETY FOR PERITONEAL DIALYSIS (ISPD)

VOLUME 15, ISSUE 2, SUMMER 2017



Importance and Prevention of Vancomycin-Resistant Enterococcus Among Peritoneal Dialysis Patients



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Vancomycin-resistant Enterococcus (VRE) is an important nosocomial pathogen which was first reported in the United Kingdom in 1980s [1]. Since then, there has been increasing incidence in VRE infection which causes outbreaks in hospitals worldwide. The clinical presentation of VRE infection can vary from simple urinary tract infection, wound infection to intra-abdominal sepsis and bacteremia.

VRE colonization is increasingly common among patients with chronic kidney disease (CKD) [2-4]. CKD patients have significant immune dysregulation compared with the general population and subsequently, have a higher susceptibility to infection. In fact, infection is the second most common cause of death after cardiovascular disease in these patients [5]. The higher rate of infection can result in extensive use of antibiotics which leads to the development of multi-drug resistant strains of micro-organisms such as VRE in these CKD patients. Although there have been studies of VRE in CKD patients, most of them were conducted in areas where hemodialysis (HD) is the main choice of renal replacement therapy (RRT). Patients receiving regular HD have frequent contacts with healthcare workers and other patients in dialysis centers. These kinds of contacts, together with the presence of vascular access, can provide a higher chance of VRE spread as well as risk of more complicated VRE infections such as bloodstream infection. As opposed to HD, peritoneal dialysis (PD) is a kind of home-based mode of RRT and vascular access is not required. As a result, we carried out a retrospective cohort study to evaluate the risk factors and the clinical outcomes of VRE colonization among the PD patients in our renal dialysis center who were hospitalized between 1st August 2013 and 31st July 2014 [6].

In this study, patients were categorized into either VRE-positive or VRE-negative groups according to the rectal swab VRE culture results. Strict contact precaution and quarantine in designated isolation ward were employed to all VRE-positive patients. Total 166 patients were included in our analysis and 28 (16.9%) of them were VRE-positive. The species of VRE identified in these patients were Enterococcus faecium. Two patients in the VRE-positive group were found to have simultaneous Enterococcus avium colonization. All the Enterococcus faecium and Enterococcus avium strains possessed the vanA resistance

phenotypes and were resistant to vancomycin according to M.I.C. in cultures. The median follow-up duration of our patients was 467 (1-759) days. Seventy-one patients developed PD-related peritonitis: 56 in VRE-negative group and 15 in VRE-positive group. None of the patients developed VRE-related peritonitis or VRE bacteremia. Only 2 VRE-related infections (1 urinary tract infection and 1 infected decubitus ulcer) were identified in the VRE-positive group. Eighty-eight patients (53.0%) died with 20 (71.4%) belonged to the VRE-positive group and 68 belonged to the VRE-negative group. There was no statistically significant difference for all-cause mortality and peritonitis free-survival between VRE-positive and VRE-negative patients. On the other hand, patients in VRE-positive group had significantly longer length of hospital stay than those in VRE-negative group. The median length of hospitalization for VRE-positive group and VRE-negative group were 17 (3-207) days and 6 (2-145) days respectively ($p < 0.01$). An important reason is probably related to the infectious control measures implemented to our VRE-positive patients. These patients could not return to their elderly home because of the strict contact precaution implementation and some of them might subsequently develop nosocomial infections, resulting in prolonged hospital stay.

Concerning the risk factors of VRE colonization, we showed that previous contact history with VRE-positive patients (OR: 417.86; 95% CI: 17.21-10147.26, $p < 0.01$), use of vancomycin in recent 3 months (OR: 130.32; 95% CI: 5.35-3176.30, $p < 0.01$) and older age (OR: 1.13; 95% CI: 1.02-1.24, $p = 0.02$) were the three independent risk factors for VRE colonization. Approximately 68% of VRE-positive patients (versus only 15.1% VRE-negative patients) had documented history of close contact with other patients with VRE colonization or infection within 3 months. Cross-transmission of VRE among patients has been well described as the cause for VRE colonization outbreak [3]. Our results suggest that meticulous infection control measures are necessary to prevent outbreak of VRE after confirming VRE colonization in our patients. Extensive contact tracing, hand hygiene, quarantining and environmental cleansing are the main domains in infection control. Moreover, exposure to vancomycin is a well-known risk factor for vancomycin resistance development in enterococci. Because of the inducible resistance phenotype, cautious use of vancomycin is necessary to prevent the emergence of VRE. In addition, use of antimicrobials such as cephalosporin and carbapenem has also been found to be associated with VRE colonization in other study [7]. An explanation is that these antibiotics damage the ecology of the gastrointestinal tract, which provides survival advantages for Enterococci, including VRE, when other risk factors such as contact history were present. As a result, minimizing the use of antibiotics, whether it is vancomycin or other antimicrobials, is important in preventing the spread of VRE.

In our study, we only included PD patients who were hospitalized. However, these hospitalized patients might have more medical comorbidities and poorer functional status. Moreover, our study was performed during an outbreak of VRE in hospitals in Hong Kong [8]. Therefore, the data may not truly reflect the real situation

of VRE colonization under normal circumstances. Further prospective large-scale studies are thus required.

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Low academic level of a patient could be overcome by intensive patient training and education in peritoneal dialysis

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As a home-based therapy, peritoneal dialysis (PD) demands patients' comprehensive understanding and management competence for PD procedure [1, 2]. These factors may relate to school education levels and socioeconomic status. In the previous studies, living in lower education area [3] or lower academic level below elementary school [4] was a risk factor for peritonitis. Academic level was associated [5] or not associated [3] with PD technique failure. In addition, academic level was associated [6] or not associated [5] with mortality. As a home-based therapy, PD relies on the patients' role more heavily than hemodialysis. Therefore, lower academic level could be a more significant issue for PD than hemodialysis. However, we have been trying to overcome the lower academic level of the patient by multidisciplinary chronic kidney disease (CKD) education and patient training. In our previous study, we have demonstrated that multidisciplinary pre-dialysis education for patients with CKD improved patient outcomes as regards infection, cardiovascular events, and urgent dialysis [7]. We recently evaluated the association between lower academic level and various patient outcomes such as mortality, peritonitis, and technique failure under a structured patient training/education system for PD patients [8].

Individualized multidisciplinary education program is offered to patients prior to starting PD in Seoul National University Hospital (SNUH). The patient and family members are educated by one-on-one lecture focused on the benefits or complications, and on outcomes of renal replacement therapy (RRT), options for RRT, dietary education, and medication education. After starting PD, patients have individualized education programs focused on PD-related procedure such as exit site care by aseptic sterilization and antibiotics ointment and exchanging dialysis fluid bag by professionally trained nurse. Among 696 patients who started PD at SNUH between January, 2000 and December, 2012, 655 incident PD patients with information on the academic background were analyzed. With respect to academic years, patients were categorized into 3 groups; middle school or lower (academic year ≤ 9 years), high school (9 years < academic year ≤ 12 years), and higher than high school (academic year > 12 years). Primary outcome was all-cause mortality analyzed using as-treated (AT) approach according to the academic groups. Besides AT analysis, post hoc intent-to-treat (ITT) analysis was also conducted in order to preclude the probability that the patients possibly having poorer outcomes might have been selectively censored by AT analysis, resulting in informative censoring. For ITT analysis, information on the mortality even after dialysis modality switch was also included in the outcome analysis. Secondary outcomes were the first peritonitis event and technique failure according to the academic groups.

A total of 655 incident PD patients (60.9% male, age 48.4 ± 14.1 years) were analyzed. Patients in higher than high school academic group were younger ($P < 0.001$). Patients supported by Medicaid service were less common in higher than high school academic group ($P = 0.038$). For AT analysis, the median follow-up duration was 41 (IQR, 20 ± 65) months. During follow-up period, 78 (11.9%) patients died. In a Cox proportional hazards model adjusted for age, gender, PD starting year, healthcare insurance status, body mass index, hypertension, diabetes, comorbidity score, visual disturbance, hemoglobin, albumin, log C-reactive protein (CRP), and estimated glomerular filtration rate (eGFR), middle school or lower academic level was not associated with all-cause mortality, as compared with higher than high school academic group (adjusted hazard ratio [HR], 1.11; 95% confidence interval [CI], 0.53-2.33; $P = 0.788$) (Figure 1)

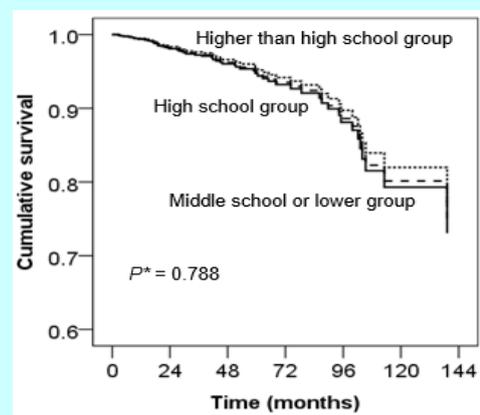


Figure 1. Overall survival of the PD patients.

(*Middle school or lower education group compared with higher than high school academic group.)

There was no significant difference in mortality among the three academic groups categorized by age <50 ($P = 0.389$) or ≥ 50 ($P =$

0.910) years. Similar result was shown in ITT analysis. Lower academic level was not associated with increased mortality ($P = 0.726$). Cardiovascular disease was the most common known cause of mortality, accounting for 33.3%. Peritonitis accounted for only 12.8% of total deaths. The causes of death were not different among the three groups ($P = 0.504$).

During follow-up period, 255 (38.9%) patients developed more than one episode of peritonitis and the average time to development of first peritonitis was 26.4 ± 27.2 months. The overall incidence of peritonitis was 0.25 episodes/patient-year. In a Cox proportional hazards models, after adjustment, middle school or lower academic group was shown to be an independent risk factor for development of peritonitis (adjusted HR, 1.61; 95% CI, 1.10-2.36; $P = 0.015$) compared with higher than high school group.

During follow up period, 138 (21.1%) patients developed technique failure and the average time to the technique failure was 41.2 ± 29.6 months. Intractable peritonitis (39.9%) and mechanical problem (15.9%) were the major causes of technique failure for all three academic groups. Competing risk regression adjusted for age and gender, middle school or lower (adjusted HR, 1.87; 95% CI, 1.10-3.18; $P = 0.038$) and high school (adjusted HR, 1.95; 95% CI, 1.29-2.95; $P = 0.002$) academic group were significantly associated with increased technique failure compared with higher than high school group.

From these results, we could conclude that lower academic level of the PD patient is a risk factor for peritonitis and technique failure. However, it was not associated with increased all-cause mortality in our PD patients under comprehensive patient training system. Therefore, patients with lower academic level may not be discouraged from choosing PD as their first line RRT. Instead, overall outcomes of the lower academic group could be improved by comprehensive training of PD exchange procedures and multidisciplinary education on the diet, blood pressure control, fluid status management, and compliance to the prescription in patients undergoing PD therapy.

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Patient-Doctor Contact Interval and Clinical Outcomes in Peritoneal Dialysis



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As a home-based form of dialysis modality, peritoneal dialysis (PD) offers inherent advantages such as preservation of residual renal function, maintenance of hemodynamics, improved quality of life, minimal requirements for medical resources and lower costs than in-center hemodialysis (HD) [1]. It is suggested that patients should return to PD centers regularly and be monitored by doctors at follow-up appointments [2,3]. The optimal contact interval however remains unknown and there is little direct evidence that more frequent patient-doctor contact (PDC) contributes to better patient outcomes in PD care.

We recently retrospectively analyzed the impact of PDC on the rate of peritonitis, hospitalization, technique failure, and mortality in patients receiving continuous ambulatory PD (CAPD) from a single center in Southern China. A total of 433 CAPD patients who lived in Guangzhou city were enrolled in this study. The mean age was 51.3 ± 15.7 years, 54.3% of patients were male, and 29.1% with diabetes. The median vintage of PD was 45.8 (26.3-69.1) months. Receiver operating characteristic curve analysis was used to calculate the sensitivity and specificity of PDC interval (area under the curve = 0.64, cut-off 2.03, sensitivity 0.60, specificity 0.60, $p < 0.001$) as a diagnostic tool for all-cause mortality in CAPD patients. We therefore defined the high PDC frequency group as PDC interval ≤ 2 months ($n = 233$, 53.8%), and low PDC frequency group as PDC interval > 2 months ($n = 200$, 46.2%). The median PDC interval was 2.0 (1.5-3.0) months in all CAPD patients, 1.5 (1.2-1.7) months in the high PDC frequency group, and 3.0 (2.4-4.0) months in the low PDC frequency group. The Charlson comorbidity index scores in the high PDC frequency group were lower than those in the low PDC frequency group ($p = 0.04$). The patients with high PDC frequency also had higher levels of hemoglobin and serum albumin after 12 months of PD therapy (all $p < 0.05$).

A total of 136 CAPD patients died during the study period. Patients with high PDC frequency had better survival rates (99.6%, 87.7% and 76.5% vs. 92.7%, 76.5% and 58.7% at 1, 3, and 5 years; $p < 0.001$). After adjustment for all confounders, PDC interval of no more than 2 months [HR, 0.60 (95% CI, 0.42-0.86); $p = 0.006$], higher levels of hemoglobin [HR, 0.98 (95% CI, 0.97-0.99); $p < 0.001$] and serum albumin [HR, 0.93 (95% CI, 0.90-0.97); $p < 0.001$] at the baseline were independently associated with better patient survival, while advanced age [HR, 1.04 (95% CI, 1.02-1.06); $p = 0.001$], higher Charlson comorbidity index scores [HR, 1.22 (95% CI, 1.09-1.37); $p < 0.001$] and baseline triglycerides [HR, 1.21 (95% CI, 1.06-1.38); $p = 0.004$] were independent risk factors for all-cause mortality in CAPD patients.

In total, 51 CAPD patients switched to HD during the follow-up period. Death-censored technique survival did not differ

significantly between the two groups (100%, 92.8% and 83.4% vs. 97.9%, 95.7% and 89.0% at 1, 3, and 5 years; $p = 0.46$). During the follow-up period, 171 (39.5%) CAPD patients experienced 338 episodes of peritonitis, 162 of which happened in 89 (38.2%) patients with high PDC frequency, and 176 in 82 (41.0%) patients with low PDC frequency. The peritonitis rate in the high PDC frequency group was lower (0.17 vs. 0.23 episodes per patient-year; $p < 0.001$). In addition, it was found that patients with high PDC frequency had shorter hospitalization time [18 (0.0-40.0) vs. 24.0 (5.0-57.0) days; $p = 0.04$] and lower hospitalization rate (0.49 vs. 0.67 episodes per patient-year; $p < 0.001$).

The suggested PDC interval for PD patients is 1-3 months in the United States and 1-6 months in China [2,4,5]. But the optimal PDC interval and its impact on clinical outcomes for PD patients remain unknown. A previous study from China showed that PDC frequency did not predict outcomes in PD patients with an integrative care strategy [4]. It was well known that experienced doctors with specialized training in PD were more likely to effectively manage peritoneal access creation, volume status, infectious complications, and cardiovascular diseases [6]. Increased PDC frequency might modify high morbidity and mortality through rapid identification and treatment of acute conditions and improved management of PD. Our study included all CAPD patients who lived in Guangzhou city and were followed up only in our PD center. The results showed that compared with CAPD patients with PDC interval of more than 2 months, patients with a lower PDC interval had better survival rates, and lower rates of peritonitis and hospitalization. They also had higher levels of hemoglobin and serum albumin after 12 months of PD. A shorter PDC interval should therefore be encouraged for PD patients to achieve better clinical outcomes.

We found that PDC interval was not associated with technique failure. This might be attributed to our comprehensive follow-up program. Training and retraining were effective in reducing the rate of PD related complications. In our study, CAPD patients and their relatives attended a standard training program following the guidelines from the International Society for Peritoneal Dialysis. During the follow-up period, patients' condition was assessed by both nephrologists and primary PD nurses through clinical visit, telephone follow-up or home visits. Retraining was offered immediately to any CAPD patient with poor compliance or worsening condition. Remote monitoring services including telephone calls, and a 24-hour telephone hotline were also available to patients. This comprehensive follow-up program may help to reduce the rate of PD-related complications, and maintain better technique survival [2,7].

In summary, this study has demonstrated that a PDC interval of 2 months or less was associated with better clinical outcomes in CAPD patients. CAPD patients with this PDC interval also had lower levels of both peritonitis and hospitalization. This indicates that a shorter PDC interval should be encouraged for PD patients to achieve better clinical outcomes.

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News from the ISPD

Join the ISPD !

Membership benefits of the International Society for Peritoneal Dialysis include:

- Print and online subscription to Peritoneal Dialysis International
- Receipt of PD News
- Online access to ISPD Guidelines
- Special registration fees at ISPD Congress, Chapter Meetings and the Annual Dialysis Conference
- Application for ISPD Scholarships and Grants

Please join the ISPD membership at www.ispd.org. There is a category of membership for developing countries (institutional membership) allowing 10 member from same institute to pay at one member cost.

Asia-Pacific Chapter Scholarship

This is a scholarship to support up to 3 months training in clinical PD for doctors and nurses from Asia-Pacific region. Deadline for application for each round: twice a year at 30 June or 31 December. **The next deadline is 31 December 2017.** Details and application procedures can be found under the Regional Chapters – Asia-Pacific Chapter, at the ISPD website.

Upcoming Meetings

23rd Annual Meeting

Japanese Society of Peritoneal Dialysis

7-8 October 2017

Kitakyushu, Fukuoka, Japan

Web site: <http://www.congre.co.jp/jspd2017/>

Biennial Australian & New Zealand Home Dialysis Conference

28 February – 2 March 2018

Auckland, New Zealand

Web site: <http://www.homedialysis2018.org>

16th Asian Pacific Congress of Nephrology

27-31 March 2018

Beijing, China

Web site: <http://www.apcn2018.org>

Abstract submission deadline: 15 October 2017

17th Congress of International Society for Peritoneal Dialysis

5-9 May 2018

Vancouver, Canada

Website: <http://ispdvancouver2018.org/>

PD First Policy in the Philippines

Dr. Mary Rose Bisquera

Head, Committee on Peritoneal Dialysis
Philippine Society of Nephrology.

The exponential growth of End Stage Renal Disease in the Philippines poses a significant stress and financial burden to our patients and their families, to the health system and to our country. The growth in the use of Peritoneal Dialysis has been slower than the increasing number of Chronic Kidney Disease patients needing dialysis. The PD prevalence varies regionally. In the developed areas, the proportion of patients on Peritoneal Dialysis generally ranges between 5 and 30%. While in our neighboring countries like Hong Kong, it is as high as 79%. However, in the Philippines, there is a continuous drop in PD utilization. A decade ago, the Philippine Renal Disease Registry has already reported a downward trend from 26% to 14%, which further decreased to the present prevalence of 4 to 6%.

The general knowledge on peritoneal dialysis is that it is simple, cheaper and cost-saving. It only requires minimal technical support and reduced need for trained technicians and nurses. PD is also advantageous to patients living in remote and rural locations as a home-based treatment option, which is ideal for patients living in an archipelago, like the Philippines.

One of the major factors that influences low PD utilization in the Philippines is the lack of financial support from the government. However, the national health insurance has recently announced the implementation of the PD First Policy to strengthen the informed decision of patients with Chronic Kidney Disease Stage 5. This policy encourages the use of peritoneal dialysis as the initial line of treatment among CKD patients requiring renal replacement therapy by favorably incentivizing this modality.

The low penetration of Peritoneal Dialysis in both the East and the West is the lack of adequate education and information of both practitioners and patients, and also the fear of infections associated with Peritoneal Dialysis. In support of the PD First Policy, the Committee on Peritoneal Dialysis of the Philippine Society of Nephrology is organizing a PD Summit. This is a three-day course for Nephrologists and nurses covering the basic principles and updates in the practice of peritoneal dialysis based on the guidelines set by the International Society for Peritoneal Dialysis. A lecture on the organization and structure of a PD program is one of the highlights of the summit. Return skills demo, PD prescription writing and case discussions are also included in the program. The aim of this summit is to guide the participants on setting up a PD Center in their areas of practice by increasing their confidence on peritoneal dialysis. The first summit is scheduled in September 2017 and this will be a regular quarterly training program open to Nephrologists and renal nurses.

With these new developments in the national health insurance coverage and the program of the Philippine Society of Nephrology, together they work with a common goal of increasing PD utilization in the Philippines.

The 6th Prof. D. G. Oreopoulos National Expert Consultation and Training Workshop on PD Related Peritonitis

The 6th Prof D G Oreopoulos national expert consultation and training workshop on PD related peritonitis was held at the Madras Medical Mission hospital Chennai India which is endorsed by the ISPD and Peritoneal dialysis society of India on 17th June 2017. The workshop was inaugurated by Prof Amit Gupta, M.D., a renowned PD expert in South Asia and he also gave the key note address. We had 120 participants and 28 resource persons (faculty) including Nephrologists, Microbiologists, PD nurses and Technologists. The primary objective of this workshop is targeted to young nephrologists and microbiologists to diagnose early ESI, catheter related infections, peritonitis and its management. The topics included basic microbiological approach to cloudy fluid, to use of Gene Xpert for diagnosis of various causative agents of peritonitis, the economic aspects of peritonitis management and switch to haemodialysis, new modalities of exit site care including use of coconut oil at exit site for prevention of ESI and nutritional challenges in peritonitis were discussed. Different patient cases with diagnostic challenges of peritonitis were presented by young nephrologists. A session for Microbiological diagnosis was the highlight and an educational quiz relating to peritonitis, catheter related infections was conducted and 4 teams of young nephrologists from different institutions took part. Cash prizes and certificates endorsed by the ISPD and PDSI were given to the I and II winning teams and the participants. The organization of the workshop was done by Dr. Anusha Rohit (clinical Microbiologist), Dr. Georgi Abraham, Dr. Milly Mathew, Dr. Deepu George and Dr. Sanjeev Nair.

Figure 1. Inauguration and lighting of the lamp.



Figure 2. The quiz team with the organizers.



Home Dialysis Conference 2018

We look forward to welcoming you to Auckland for the Home Dialysis 2018 Conference. www.homedialysis2018.org
The Home Dialysis Conference will bring together health care professionals from NZ, Australia and the Pacific focussing on building and developing home based dialysis therapies.



The banner features a logo on the left consisting of a blue house shape with a red kidney symbol inside. To the right of the logo, the text reads: "Biennial Australian & New Zealand HOME DIALYSIS CONFERENCE AUCKLAND 28 FEB-2 MAR 2018 Building For Home". Below the logo and text is a photograph of the Auckland city skyline at night, with the Sky Tower prominently visible. The text "Registrations Open" is centered over the skyline, and the website address "www.homedialysis2018.org" is at the bottom.

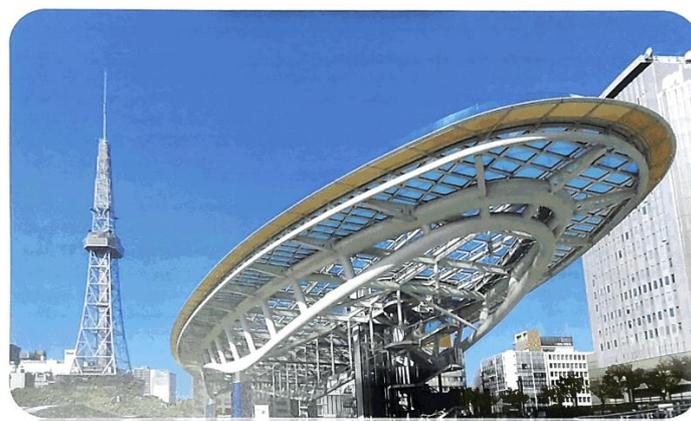
Key Dates

- Early bird registration opens – 01 June 2017
- Call for abstracts (orals and posters) – 16 June 2017
- Early bird registration closes – 31 October 2017
- Call for abstracts closes – 31 October 2017
- Notification to the authors – 30 November 2017



The banner has a blue background on the left with the APCN 2018 logo, which is a white circle containing a kidney shape and the text "APCN 2018". To the right of the logo, the text reads: "2018 ASIAN PACIFIC CONGRESS OF NEPHROLOGY 2018亚太地区肾脏病学术会议". Below this, it says "27-31 March, 2018 China National Convention Center, Beijing, China" and "2018年3月27-31 中国·北京 国家会议中心". The right side of the banner features a scenic view of a traditional Chinese pagoda on a hillside with misty mountains in the background.

9th Asia Pacific Chapter Meeting of International Society for Peritoneal Dialysis



In Nagoya, Japan
2019