# EPIDEMIOLOGICAL STUDY OF THE PERITONEAL DIALYSIS PROGRAM IN NEPAL, COMPARISON TO OTHER REGIONS, CHALLENGES AND OPPORTUNITIES TO STRENGTHEN PERITONEAL DIALYSIS ACTIVITY IN THE SOUTH ASIAN REGION

## PhD thesis

Klára Paudel

Doctoral School of Theoretical and Translational Medicine Semmelweis University





Supervisor:

Ágnes Haris, Ph.D

Official reviewers:

László Wagner, Ph.D Péter Vörös, Ph.D

Head of the Complex Examination Committee: György Reusz, D.Sc Members of the Complex Examination Committee: András Tislér, Ph.D Csaba Ambrus, Ph.D

Budapest 2021

## Introduction

Renal replacement therapy (RRT) has placed significant burden on all types of health care systems in the world. It requires lifelong commitment with high cost and multiple co-morbidities complicate the care of these patients. Peritoneal dialysis (PD) offers cost-saving not only in medical equipment and manpower, but due to being a home-based therapy, offers higher quality of life. Especially during the current COVID-19 pandemic, avoidance of frequent hospital visits is an important benefit. Despite the clear advantages, PD utilization is limited in most developing countries, while hemodialysis (HD) is growing.

Continous ambulatory peritoneal dialysis (CAPD) was established initially in the 1970's. After the introduction of the Y-shaped connecting system and the flush before fill technique, it became more widely utilized in the world.

Nepal is located in the South Asian region with 29.1 Million population. It is currently a lower-middle-income country, and 79.85% of the population live in rural areas. Health care in Nepal has significant out-of-pocket expenses due to lack of universal health insurance. In Nepal acute intermittent PD was practiced from 1971 and CAPD from 1992, however the first sustained program was started from 2002. Hemodialysis (HD) was very limited in Nepal until 2013, after the introduction of government supported dialysis it started expanding. From 2013 free HD and from 2014 free PD is available for Nepalese citizens, however HD still has significant capacity deficit. There are 60 nephrologists in Nepal and 80% of them are located within the capital. Among the 65 dialysis units in Nepal, 22 are government

owned, 8 belong to non-profit charity organizations, 10 are in teaching hospitals and 25 are private units. Among these, only 10 centers practice PD.

# Objectives

In our research we try to answer the following questions, by examining the PD practice in Nepal and in South Asia:

- 1. What are the PD practices in Nepal?
  - a. Demographics and educational background of Nepalese PD patients
  - b. PD Catheter types and methods of implantation in Nepal
  - c. Transport status and number of exchanges in PD in Nepal
  - d. Complications and outcomes of PD in Nepal
  - e. Indications and motivating factors to choose PD
- 2. What are the differences between PD and HD patients in Nepal, in terms of basic characteristics, quality of life and fluid balance?
- Are the PD practices in Nepal different than in other countries or regions? We compare available data about RRT and PD practices from other countries and regions with data from Nepal.
- 4. What are the main challenges and opportunities to strengthen PD programs in low-resource settings, such as Nepal and other South Asian countries?

## Methods

For data collection the following sources and methods were used:

- 1. Nepal Government, Health Services Department, Free Dialysis Scheme reimbursement records
- PD clinical coordinator's records of patients from the Kathmandu valley between 2012 2016
- 3. Interviewing PD patients from multiple centers
- 4. Peritoneal dialysis patients registry between 2014-2021 at Pokhara
- 5. Inteviewing HD patients in the Pokhara region about causes of CKD
- 6. Interview of HD and PD patients from two centers in Pokhara about quality of life and fluid balance

For statistical analysis SPSS 26.0 software and the PD.excel software was used. Differences between patient groups were analyzed by independent samples t-test and Mann-Whitney U test, for normally distributed and for non-parametric data, as appropriate. Technique survival and patient survival data was assessed by Kaplan-Meier analysis and log rank test. Categorical variables were expressed as percentage and groups were compared by Chi-square tests. All tests were two-tailed and p-values of < 0.05 were considered significant.

## Results

### **Characteristics of PD patients in Nepal**

In Nepal, among 4398 prevalent dialysis patients 177 (4%) were on CAPD in 2018. Among 236 PD patients, majority of patients were 40-65 years old (47%) and 68% was male. Among these PD patients 53% had diabetes mellitus, other common primary kidney disease were glomerulonephritis, hypertension and interstitial nephritis. Illiterate were 21% and 50% completed primary or secondary school. Double-cuff Tenckhoff catheter is used in all centers, 3 centers practice percutaneous insertion with Seldinger method, others use surgical insertion. In Pokhara among 88 PD catheter insertions, 83 were done via percutaneous method and 5 primary surgical, 6 started as percutaneous and converted to surgical. Complications were early outflow problem in 10.8% that self-resolved in 6%. Surgical repositioning was required in 2.4% and 2.4% dropped out of PD.

Transport status of PD patients in Nepal based on 53 available PET test result: low transporter 3.7%, low average 35.8%, high average 49,0%, high transporter 11.3%. Majority of PD patients (89.8%) use daily 3 exchanges of 2 liter fluids. Daily 4 bags are used by 3% and daily 2 bags by 5.1% of the PD patients. Peritonitis rate was 1:41 in 2015 in Kathmandu, in Pokhara it was 1:19 in the first year, later 1:29. The one-year survival rate between 2012-2015 in Kathmandu was 87% and the one-year technique survival rate was 81%. Most patients chose PD for better quality of life, long distance of home from dialysis center and unavailability of HD seats.

## Comparison of PD and HD patients in Pokhara

In Pokhara 219 HD and 88 PD patients' basic characteristics were compared. Age and gender ratio were not different, among PD patients there were more rural patients and more patients had diabetes in history. 25 and 26% of patients had a history of working abroad. We compared PD vs. HD patients' Health Related Quality of Life (QoL) with the help of Short Form 36 (SF-36) questionnaire. Physical functioning, physical role, bodily pain and social functioning domains showed significantly higher scores in the PD patient cohort and none of the SF-36 QoL domain performed worse in the PD group compared to the HD group. Among the HD population a subanalysis was done based on fluid balance. Patients with low interdialytic weight gain (IDWG) had higher QoL scores, especially in the physical functioning, physical role and emotional role domains.

#### Comparing data from Nepal to other parts of the world

We compared data from Nepal with data from Hungary, Europe and USA, using the Hungarian data by Kulcsar et al., ERA-EDTA and USRDS registry data. Mean age was significantly lower in Nepal than in any other regions (46.7 vs 55.0 – 65.4 years). Similarly, male ratio was significantly higher (64-70% vs 58.3-60%). PD rate was 8-13% among these countries, compared to 4% in Nepal. Outcome data was compared with data from Sweden and South Korea, showing comparable results (87% vs. 91.9-94.9%). Motivating factors were compared with survey results from Taiwan and Switzerland, where patient comfort and right to choose, survival benefit and other ethical issues play a part and the financial aspects are less

important. In the low-resource settings capacity, availability and affordability plays the major role.

### Comparing data from Nepal with the South Asian region

Prevalence rate for CKD is highest in Nepal, however, this data includes all stages of CKD, not only ESRD. Pakistan and Bangladesh have the lowest number of nephrologists per million population (0.7/million) and Nepal has the highest number among these countries (2.1/million). Access to dialysis is limited in all of the five countries, making it average less than 20-25% of the population. Pakistan has the lowest number of patients on dialysis compared to population (90 patients/million population) and Sri Lanka has the highest number (256 patients/million population). PD utilization is highest in Sri Lanka with 7% of the total dialysis population and lowest in Pakistan with 0.4%.

# Challenges and opportunities to strengthen PD programs in the South Asian region

The major issues limiting the development and growth of PD programs include problems with staff training and retention, patient concerns and issues, maintenance of a reliable supply of fluids, and adequate financial support. While trying to establish a PD program, the following key points need to be addressed: manpower, which includes three main areas – doctor, nurses or clinical coordinators and surgeon; secondly, institutional and health care system factors. These include stable fluid supply and financial support, since many developing countries have no stable health insurance system and patients have large out-of-pocket expenses.

## Conclusion

This thesis has demonstrated an example on a PD program in Nepal, a low-resource setting area among the developing countries. We found, that demographics of the PD population are different to other developed countries especially in terms of age, gender distribution and primary renal diseases. Catheter types are same as in other places, especially the Tenckhoff catheters used, but insertion technique varies between centers based on the experience and skills of the nephrologists. In Nepal, most patients use less exchanges compared to other developed countries, namely 3 exchanges per day, which is feasible as patients have lower body mass and can achieve a fairly adequate clearance. The one-year patient survival rate is comparable to other developed countries. Peritonitis rate was higher than the recommended ISPD target, and the monitoring of peritonitis rate is also lacking. We have shown, that the indications and motivating factors to choose PD can be different from other developed countries, especially because capacity, affordability and availablity plays major roles in the selection of RRT options. In Nepal the nephrologist to population ratio is very low and they are overwhelmed by the workload, thus proper documentation and monitoring might be lacking in most centers.

In this thesis we also explored the possible challenges while trying to establish a PD program in a low-resource setting. It is demonstrated, that two main areas need to be addressed, first, the manpower which needs to be trained and skilled, namely – doctors, nephrologists, nurses, technicians, coordinators, and surgeon. Another two key factors are the fluid supply that needs to be stable and reliable with good quality products and the financial

support from government or insurance. The thesis provides practical advices on how to overcome these challenges, especially with tables that demonstrate these step by step.

PD is an important part of RRT programs in the world but sadly it is represented in very low numbers in most places. We need to explore all possibilities to promote this modality.

## **Candidate's List of Publication**

## Related to the theme of the PhD thesis

- Overcoming barriers and building up a strong CAPD program experience from three South-Asian countries. Paudel K, Qayyum A, Wazil AWM, Sharma SK, Shrestha K, Fan S, Haris A, Finkelstein FO, Nanayakkara N. Perit Dial Int. June 2. 2021 <u>https://doi.org/10.1177/08968608211019986</u> Impact factor: 1.768
- 2. Peritoneal dialysis catheters, insertion methods and complications. **Paudel K**. Pak J Kidney Dis 2020;4(supplement 1):13-20.
- Peritoneal dialysis in Nepal: history, current situation and challenges. Paudel K, Sharma SK, Chhetri PK, Shah DS, Manandhar D, Shrestha K, Kafle RK, Paudel B, Basnet R, Adhikari S, Haris A. Indian J Perit Dial 2018;35(2):19-24.
- 4. Successful management of Acute Kidney Injury with peritoneal dialysis in a patient after heart transplantation with Burkholderia septicemia. **Paudel K**, Rudreshwar P, Rajeevalochana P et al. Indian J Perit Dial 2016;31(2):38-42.
- 5. How to overcome barriers and start up new peritoneal dialysis programs experience from Nepal. **Paudel K**, Fan S, Sharma S, Shrestha K. Nephrol Dial Transpl. 2016;31(suppl1)i503
- 6. Can Bioimpedance Measurements of Lean and Fat Tissue Mass replace Subjective Global Assessments in Peritoneal Dialysis Patients? **Paudel K**, Visser A, Burke S, Samad N, Fan SL. Journal of Renal Nutrition. 2015;25(6):480-487. **Impact factor: 1.871**

- Increasing the use of biocompatible, glucose-free peritoneal dialysis solutions. Qayyum A, Oei EL, Paudel K, Fan SL. World J Nephrol 2015;4(1):92-97.
- Comparing lung ultrasound with bioimpedance spectroscopy for evaluating hydration in peritoneal dialysis patients. Paudel K, Kausik T, Visser A, Ramballi C, Fan SL. Nephrology 2015;20:1-5. Impact factor: 1.864
- Lack of motivation a new modifiable risk factor for peritonitis in peritoneal dialysis patients? Paudel K, Samad N, Namagondlu G, McKitty K, Fan SL. Journal of Renal Care. 2015;41(1):33-42.
- Is overhydration in Peritoneal Dialysis patients associated with cardiac mortality that might be reversible? EL Oei, K Paudel, A Visser, H Finney and SL Fan. World J Nephrol 2016;5(5):448-454.
- Is there an end in sight for encapsulating peritoneal sclerosis?
  Paudel K, Fan SL. Perit Dial Int 2014;34:576-578. Impact factor: 2.097
- Successful use of continuous ambulatory peritoneal dialysis in 2 adults with a gastrostomy. Paudel K, Fan LS. Am J Kidney Dis. 2014;64(2):315-318. Impact factor: 5.294
- 13. The first report of the Hemodialysis Registry of the Western Region of Nepal. **Paudel K**, Paudel B. Poster presentation at WCN 2013, Hong Kong.
- Prevalence of hypothyroidism in a CKD population undergoing maintenance hemodialysis. Paudel K. J Clin Diag Research 2014; 8(4): MC01-MC04.

## Unrelated to the theme of the PhD thesis

- Role of elimination diet in the management of proteinuria. Paudel K. J Renal Nutr Metab 2019;5:41-3.
- Diagnostic significance of Holter monitoring in the evaluation of palpitation. Paudel B, Paudel K. J Clin Diag Research 2013;7(3):480-3.
- Autoimmune thyroiditis: clinical presentation in a Nepalese population. Paudel K, Paudel B. Nepal J Med Sciences 2014; 3(1): 44-47.

- A study on the sensitivity pattern of UTI pathogens in the Western Region of Nepal. Paudel K, Paudel B. J Gandaki Med Coll 2010; 3(1): 27-31.
- Hemodialysis at Charak Hospital and Research Center the first year's experience. Paudel K. J Gandaki Med Coll 2009; 2(4): 24-27.
- Myocarditis and Mobitz Type I Heart Block Following Wasp Sting. Vishwanath P, Adhikari D, Akila, Paudel R, Paudel K, Pillay VV, Menezes RG. Internet J Card 2010;8(1)
- Western Nepal acute coronary syndrome (WestNP-ACS) registry: Characteristics, management and in- hospital outcome of patients admitted with acute coronary syndrome in western Nepal. Paudel B, Paudel K. J Gandaki Med Coll 2009; 2(3):51-59.
- Evaluating chronic cough: causes and consequences. A study conducted in Charak Hospital and Research Center, Pokhara, Nepal. Paudel B, Koirala T, Paudel K and Dhakal B. J Gandaki Med Coll 2009; 2(2):53-59.
- A study of wasp bites in a tertiary hospital of western Nepal. Paudel B, Paudel K. Nepal Med Coll J. 2009;11(1):52-56.
- 24. Acute coronary syndrome in elderly the difference compared with young in intensive care unit of a tertiary hospital in western Nepal. Paudel R, Panta OB, Paudel B, **Paudel K**, Pathak OK, Alurkar VM. J Clin Diag Research 2009;3(1):1289-1296.
- Clinical predictors of successful thrombolysis with streptokinase and possible circadian periodicity. Paudel B, Paudel K, Panta OB. J Gandaki Med Coll, 2008; 1(2):50-60.
- Parkinsonism with Shy-Drager syndrome--a case report. Paudel B, Paudel K, Paudel R, Pandru K. Nepal Med Coll J. 2008;10(1):68-71.
- 27. A study of acute coronary syndrome in western region of Nepal. Paudel B, **Paudel K**, Paudel R, Shrestha G, Maskey A, Panta OB. J Gandaki Med Coll. 2008;1(1):

# Acknowledgements

I would like to give thanks to my mentor, Dr Agnes Haris for her professional guidance, support and continuous encouragement in bringing this work forward. I also give thanks to Prof. Laszlo Rosivall who generously accepted me in this journey of the PhD school.

I also would like to give thanks to Dr Stanley Fan, my mentor during my ISN fellowship at Barts Health NHS, who constantly guided and instilled in me the love for peritoneal dialysis and research.

I am enourmously thankful to my husband, Dr Badri Paudel, who always stands by my side and encourages me to aspire higher and never get tired.

I am thankful to Mrs Rachana Basnet, in-charge of nursing at Charak Memorial Hospital, Pokhara, who tirelessly helped in all our research projects and was the one who always remembered to complete the tasks on time.

I am thankful to my mother, Istvanne Belasitz, who blesses my life every day with love and care, and who encourages me to become better. I am thankful to my father, Istvan Belasitz, who was always by my side during my school years and was my first biggest fan and cheered me up during the hard times. I know he is cheering and looking at me from the other side of the veil now as well.

I am endlessly thankful to my dear mother-in-law, Janaki Paudel, who tirelessly works and supports our family, who enabled me to get back to work and have a full value professional life despite the responsibilities as a mother of three children.

I am thankful to my patients and my collegues for believing in me and supporting in all aspects of life.

I would like to say thanks to all my friends and family members for the encouragement, patience and acceptance, that helped to envision and execute this work.

Dr Klara Paudel Pokhara, Nepal 25<sup>th</sup> July 2022