JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY

2021 Volume 1 • eISSN 2710-5903

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

MALAYSIAN SOCIETY OF NEPHROLOGY

ORIGINAL ARTICLES

Original Research

1. A Retrospective Study on the Incidence and Outcomes of Acute Kidney Injury among Patients Diagnosed with Malaria Infection in Sabah – a Tertiary Centre Experience

Alexander Kok Yip Chow, Nadirah Sulaiman, Khai Lip Ng, Sooth Jiun Lu, Valerie Scarlett Seibing, Koh Wei Wong

Case Report

2. The usage of guidewire or stylet in successful peritoneal dialysis catheter exchange without fluoroscopy or peritoneoscope use - The Serdang Method

Azhar Azhani, Christopher Thiam Seong Lim, Bak Leong Goh

3. Acute bilateral basal ganglia lesion: Lentiform fork sign in end stage kidney disease with metabolic acidosis

Lau Siew Ping

JOURNAL OF CLINICAL AND
TRANSLATIONAL NEPHROLOGY (JCTN)

ACKNOWLEDGEMENT

TO REVIEWERS

The Editors gratefully acknowledge the assistance of the following people, who spent valuable time reviewed submitted manuscripts for the current issue of Journal of Clinical and Translational Nephrology (JCTN)

1. Professor Dr Abdul Halim Gafor
2. Dr Sunita Bavanandran
3. Dr Lily Mushahar
4. Dr Ravindran Visvanathan
5. Dr Nor Fadhlina Binti Zakaria
6. Dr Ng Eng Khim
7. Dr Liu Wen Jiun
8. Dr Rosnawati Yahya
9. Dr Anim Md Shah

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Case Report

Open Access

A RETROSPECTIVE STUDY ON THE INCIDENCE AND OUTCOMES OF ACUTE KIDNEY INJURY AMONG PATIENTS DIAGNOSED WITH MALARIA INFECTION IN SABAH – A TERTIARY CENTRE EXPERIENCE

Alexander Kok Yip Chow[1], Nadirah Sulaiman[2], Khai Lip Ng[3], Sooth Jiun Lu[1], Valerie Scarlett Seibing[3], Koh Wei Wong[1]

[1] Nephrology Unit, Department of Medicine, Hospital Queen Elizabeth, 13a, Jalan Penampang, 88200 Kota Kinabau, Sabah.
[2] Clinical Research Centre, Hospital Queen Elizabeth, 13a, Jalan Penampang, 88200 Kota Kinabau, Sabah.
[3] Department of Medicine, Hospital Queen Elizabeth, 13a, Jalan Penampang, 88200 Kota Kinabau, Sabah.

ABSTRACT

Introduction: Malaria infection is frequently complicated with acute kidney injury (AKI). Malaysia has an unique epidemiology – its malaria infections are primarily caused by the simian parasite *Plasmodium knowlesi*. Data is lacking on the incidence of AKI in *P. knowlesi* infection. Previous studies have suggested that *P. knowlesi* is associated with more severe features compared to *P. falciparum*.

Methods: We conducted a one-year retrospective cohort study to assess the incidence and outcomes of AKI among patients admitted for malaria infection at a state tertiary hospital.

Results: A total of 173 admissions for malaria infection was reported in Queen Elizabeth Hospital, Sabah in 2018. We excluded 53 cases from final analysis as clinical notes were unavailable. *Plasmodium knowlesi* infection was the organism reported in 97.5%. 19.2% (23/120) were classified as severe malaria. 31.7% (38/120) developed AKI as per KDIGO criteria. All incidences of acute kidney injury occurred within 48 hours of admission. After ruling out other causes, they were all attributed to be secondary to malaria infection. Among those with AKI, majority (50%) were Stage 1, 29% were Stage 2, while 21% had stage 3 acute kidney injury. 7.8% required temporary haemodialysis. Renal function normalised in 81.6% of AKI patients upon discharge. At 3 months followup, 13% of AKI patients had persistent renal impairment, with eGFR ranging from 44.2 – 51.9ml/min/1.73m2. Multivariate analysis showed that age more than 50 years old (OR 3.25; CI 1.37, 7.73; p=0.008), and high total bilirubin count (OR 5.6; CI 1.73, 18.12, p=0.004) were associated with the development of AKI.

Conclusion: AKI is common in malaria secondary to *Plasmodium knowlesi* infection. 13% of patients with AKI had persistent renal impairment at 3 months followup.

Keywords: *Malaria, Acute Kidney Injury, Plasmodium knowlesi*

**Corresponding author:*
Alexander-Kok Yip Chow
Nephrology Unit, Department of Medicine
Hospital Queen Elizabeth, Sabah, Malaysia.
Email address: alexchowky@yahoo.com

JCTN (2021) Volume 1: Article no: 1

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

INTRODUCTION

The World Health Organisation (WHO) estimated that in 2016, 216 million cases of malaria occurred worldwide, among which 7% occurred in the South-East Asia region. This amounted to 15 million cases yearly (1). Malaria can be caused by any of the five *Plasmodium* species, namely, *Plasmodium falciparum, Plasmodium ovale, Plasmodium malariae, Plasmodium vivax*, and *Plasmodium knowlesi.*

Malaysia has an unique epidemiology – its malaria infections are primarily caused by the simian parasite *Plasmodium knowlesi* (2). This is not reported in other localities. Previous studies have suggested that *P. knowlesi* infection is associated with more severe features compared to *P. falciparum* infection (3).

Acute kidney injury (AKI) is a well-documented complication of malaria infection and it is associated with a higher case fatality rate (4,5). Globally reported incidences of AKI in malaria vary greatly, from 8% to 17.6% (6,7). In Southeast Asia, AKI is one of the most common complication in adults with *P. falciparum* malaria (8). A prospective study in west Pahang, Malaysia, has shown that malaria accounted for 3.3% of AKI in tropical acute febrile illness (9). A single centre report by a local tertiary hospital demonstrated AKI in 17.1% of patients diagnosed with malaria, among which 7.7% required dialysis (10).

There is a dearth of data on the incidence of AKI among *P. knowlesi* infection, as well as their long-term renal outcomes.

We reviewed all cases of malarial infection admitted to Queen Elizabeth Hospital from 1st January 2018 to 31st December 2018. We aim to assess the incidence, severity, and outcomes of AKI, as well as to identify any associations between sociodemographic or clinical factors and the occurrence of AKI.

MATERIALS AND METHODS

Queen Elizabeth Hospital (QEH) is an 800 bedded, tertiary care hospital located at the Malaysian state of Sabah, which serves a population of 3.9 million (11). As the main referral hospital in the region, it is funded by the Ministry of Health, and is equipped to provide intensive care service, renal replacement therapy services, and subspecialty consultations. The Malaysian Prevention and Control of Infectious Disease Act 1998 mandates notifying and reporting of all cases of malarial infections upon diagnosis. Upon research and ethical approval, the identifying particulars of all patients diagnosed with malaria infection and admitted to Hospital Queen Elizabeth during the study period (1st January 2018 to 31st December 2018) were retrieved from the Sabah State Health Department.

In the year 2018, QEH reported a total of 173 cases of malarial infection. They were all hospitalised, as per local protocol. Patient's clinical features upon initial presentation to any healthcare facility, blood investigations, and in-hospital ward allocation and progress were recorded. We excluded patients who were less than 18 years old, patients on regular renal replacement therapy and patients with history of renal transplant. This study was approved by the Malaysian Medical Research Ethics Committee (MREC).

DEFINITIONS

1. Acute kidney injury (AKI)

AKI is an acute reduction in kidney function, diagnosed via changes in serum creatinine and/or urine output. It is defined as a rise of serum creatinine of equal or more than 26.5μmol/L within 48 hours, or an increase in serum creatinine of equal or more than 1.5 times of baseline level; or urine volume of less than 0.5ml/kg/hour for 6 hours. The increase of serum creatinine from baseline must occur within prior 7 days(12). We classify severity of AKI based on the KDIGO classification (12). Patients with AKI will also be sub-classified into whether renal replacement therapy was required during the hospital stay.

The diagnosis of AKI requires the demonstration of rising serum creatinine trend. Since patients who present with an abnormal serum creatinine may not have a known baseline serum creatinine, a diagnosis and staging of AKI based on change of creatinine from baseline poses a limitation. We adopted the method described by the Acute Dialysis Quality Initiative (ADQI) group (13), whereby in patients without a baseline serum creatinine level, a normal premorbid renal function is assumed (GFR: 75ml/min/1.73m^2). The baseline creatinine level is then back calculated using the Modification of Diet in Renal Disease (MDRD) formula. This method has been used in previous studies (6).

In patients with confirmed AKI, serial creatinine taken in the ward would be recorded. We looked at onset of AKI after admission to determine whether it is a community-acquired (onset <48 hours after hospitalisation) or hospital-acquired AKI (onset after 48 hours of admission). We also took into consideration the clinical presentation, in an attempt to rule out other causes of AKI before deeming the AKI to be due to malarial infection. In patients who had persistent elevated/abnormal serum creatinine upon

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

discharge, blood tests were done at 1 month and 3 months after discharge, to look for renal recovery (normalization of serum creatinine levels). The estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula. Patients with an eGFR of less than 60ml/min/1.73m^2 at 3 months after discharge are deemed to have developed chronic kidney disease (CKD). They were subsequently staged as per KDIGO criteria (14)

2. Severe malaria

Severe malaria is diagnosed based on the criteria outlined by the World Health Organisation (WHO) in 2015 (15).

STATISTICAL ANALYSIS

Data were extracted from hospital case notes and computed into Statistical Package for Social Sciences (IBM Corp. Released 2013. IBM Statistics for Windows, Version 22.0. Armork, NY: IBM Corp.) for data analysis and interpretation.

Logistic regression was used to assess for factors associated with AKI. Univariate logistic regression was used to determine the unadjusted odds ratio between exposure variables and status of AKI. The simultaneous effects of capillary blood sugar, peripheral capillary oxygen saturation, age, respiratory rate, white blood cell count, aspartate transaminase (AST), total bilirubin, systolic and diastolic blood pressure, haemoglobin, platelet, serum bicarbonate and AKI status were determined via multivariate logistic regression analysis. Using automatic variable selection procedures, we identified significant factors by fitting all independent variables of interest into the model. We applied both forward and backward stepwise variable selection procedures with P value less than 0.05 as significant variable to include into the model. The assumptions of linearity in logit for each continuous variable were checked. The selected continuous variables linearity assumption was not met, thus the variables were categorized. The selected model in this step was considered preliminary main-effect model. Next, two-way interactions between selected independent variables were checked. The preliminary main-effect model was also checked for multicollinearity problem by obtaining variance-inflation-factor (VIF) for each independent variable. Goodness-of-fit statistics was used to assess the fit of the logistic model against the actual outcomes. Adjusted odds ratios and 95% confidence intervals were estimated. The P-value of 0.05 is considered significant.

RESULTS

Patient Characteristics

Queen Elizabeth Hospital reported 173 cases of malaria infection in the year 2018. Fifty three cases were excluded from analysis as case notes were incomplete or unavailable. Data analysis was done on the remaining 120 cases. The baseline demographic and clinical features upon presentation are summarised in Table I. Patients have a mean age of 43.5 years, predominantly male gender (83.3%), and are *Sabahan Bumiputras* in ethnicity (95%), Chinese (3.3%) and non-Malaysian (1.7%).

Table I: Baseline Demographic and Clinical Features upon Presentation to Hospital

Variables	
Age, years	43.5 (18.0)
Gender - Male - Female	 100 (83.3) 20 (16.7)
Ethnicity - *Sabahan Bumiputras* - Chinese - Others	 115 (95.0) 4 (3.3) 2 (1.7)
History of Malaria infection	14 (11.7)
Underlying medical comorbidities	34 (28.3)
Duration of unwell, days	5.7 (2.8)
Use of nephrotic drugs	8 (6.7)

JCTN (2021) Volume 1: Article no: 1

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

Table I: Baseline Demographic and Clinical Features upon Presentation to Hospital *(cont').*

Source of patient - Walk-in - Referred from district hospitals	 22 (18.3) 98 (81.7)
Malaria species - Plasmodium knowlesi - Plasmodium falciparum - Plasmodium vivax - Co infection (P knowlesi + P malariae)	 117 (97.5) 1 (0.8) 1 (0.8) 1 (0.8)
Severe malaria	23 (19.2)
Initial antimalarial treatment - Intravenous arthesunate - Oral riamet (artemether, lumefantrine) - Oral chloroquine and Intravenous clindamycin	 64 (53.3) 55 (45.8) 1 (0.8)
Patient disposition upon admission - Intensive care/High dependency ward - General ward	 18 (15.0) 102 (85.0)
Inotropic support on admission - No inotrope - One inotrope	 109 (90.8) 11 (9.2)
Intubation	1 (0.8)
Duration of hospitalisation, days	4 (2)
Systolic blood pressure, mmHg	120.2 (19.0)
Diastolic blood pressure, mmHg	70.8 (12.3)
Heart rate, beats per minute	96.6 (17.4)
Temperature, °C	38.0 (1.2)
Respiratory rate, breaths per minute	19.1 (2.6)
SPO2, %	98.2 (2.72)
Parasite count, parasites/µL	22126.56 (56156.4)
Haemoglobin, g/dL	13.2 (1.7)
White blood cell count, 10^3/µL	7.0 (2.3)
Platelet count, 10^3/µL	73.7 (85.5)
Creatinine, µmol/L	96.0 (74.5-115.6)**
Total bilirubin, µmol/L	29.7 (19.6)
Aspartate transaminase, U/L	45.5 (28.7)
Alanine transaminase, U/L	57.6 (44.1)
pH	7.4 (0.1)
Serum bicarbonate, mmol/L	23.3 (3.9)
Serum lactate, mmol/L	1.7 (0.8)
Capillary blood sugar level , mmol/L	6.9 (2.1)

**Continuous variables are described as Mean (+/- Standard Deviation), and categorical variables as n(%).*

*** median (IQR)*

JCTN (2021) Volume 1: Article no: 1

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

This cohort of patients were relatively well, with only 28.3% reported as having one or more underlying medical comorbidities. They presented after a mean of 5.7 days after feeling unwell. Most of the cases were referrals from district hospitals (81.7%). 11.7% volunteered a history of malaria infection. Eight cases (6.7%) had history of nephrotoxic drug consumption one week prior to presentation.

The majority of malaria infection is due to *P. knowlesi* (97.5%). One fifth (19.2%) of patients has severe malaria, as defined by WHO in 2015 (15). The main criteria used for diagnosis of severe malaria were shock (34.8%), acidosis (21.7%) and renal impairment (21.7%). They were hospitalised for a median of 4 days. There was no mortality reported in year 2018.

After admission, most of the patients were admitted to the General Ward (85%). Eighteenpatients were admitted to Intensive Care Unit (ICU). Artesunate (53.3%) was the most common initial antimalarial therapy given to the patients, followed by Riamet (Artemether/Lumefantrine) (45.8%) and Chloroquine plus Clindamycin (0.8%). During the clinical progression, only one patient has been intubated, whereas 11 patients required one inotropic support.

INCIDENCE OF AKI AND RENAL OUTCOMES

The median serum creatinine on presentation was 96.0µmol/L (IQR 74.5-115.6). Among the 120 cases analysed, 38 patients (31.7%) developed AKI based on KDIGO classification (Figure 1). All incidences of acute kidney injury occurred within 48 hours of admission. After ruling out other causes, they were all attributed to be secondary to malaria infection.Among those who developed AKI, 19 (50%) developed Stage 1, 11 (29%) developed Stage 2, and 8 (21%) developed Stage 3 AKI. Among those who developed Stage 3 AKI, 3 (7%) patients required temporary inpatient haemodialysis. One patient's renal function normalized at 1 month of follow-up, while 5 patients had persistent renal impairment at last review 3 months after discharge. Their eGFR ranged from 44.2 to 51.9ml/min/1.73m^2, which corresponds to CKD Stage 3.

FACTORS ASSOCIATED WITH AKI

Univariate analysis revealed patients who developed AKI were significantly older. On presentation, patients who developed AKI had significantly lower blood pressure, and a higher respiratory rate. Patients who developed AKI were also significantly more likely to have lower haemoglobin, higher white blood cell count, lower platelet count, higher total bilirubin, higher aspartate transaminase (AST) level, and lower serum bicarbonate. They are more likely to be admitted to the intensive care unit, and to be on inotropic support. There is no association between parasite load and incidence of AKI. (Table II).

Multivariate analysis showed that increasing age and elevated bilirubin conferred additional risk to the development of AKI. (Table III). The model fits well (Hosmer and Lemeshow test p= 0.934) and 71.4% of cases are predicted correctly if they have AKI or not. Area under the curve of receiver operating characteristic is 71.6% which indicate acceptable discrimination of the model's ability to discriminate between the two outcomes.

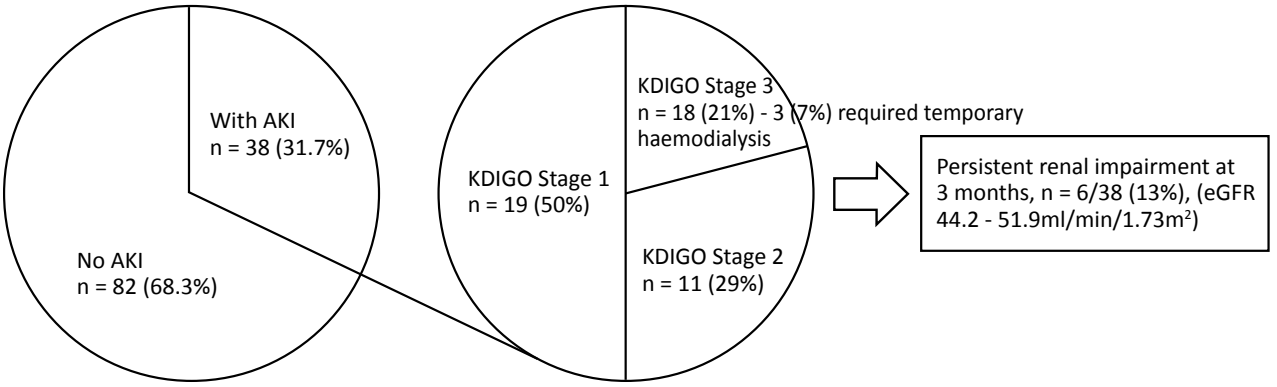


Figure 1: Incidence of AKI, severity and renal outcomes.

Table II: Selected factors associated with AKI by univariate analysis

Parameters	n	% with AKI	Unadjusted OR (95% CI OR)	P-value[a]
Gender - Male - Female	 100 20	 35 15	 3.05 (0.84, 11.13) 1	0.091
History of malaria - Yes - No	 14 106	 21.4 33	 0.55 (0.15, 2.11) 1	0.386
Comorbidities - Yes - No	 34 86	 44.1 26.7	 2.16 (0.94, 4.95) 1	0.068
Nephrotoxic drug - Yes - No	 8 112	 50 30.4	 2.29 (0.54, 9.71) 1	0.259
Inotropes - Yes - No	 11 109	 63.6 28.4	 4.40 (1.20, 16.01) 1	0.025
Intubated - Yes - No	 1 119	 100 31.1	 3.58 x 109 (0.00, -) 1	1.000
Patient disposition upon admission Intensive care/high dependency ward General	 18 102	 77.8 23.5	 11.38 (3.42, 37.83) 1	<0.001
Heart rate, beats per minute			1.00 (0.98, 1.02	0.922
Temperature			1.04 (0.76, 1.42)	0.830
Duration of unwell, days			1.02 (0.89, 1.16)	0.830
Parasite count			1.00 (1.00,1.00)	0.117
pH			1.26 (0.001,2.17x103)	0.952
Lactate			1.70 (0.88, 3.26)	0.112
SPO2			0.75 (0.61, 0.92)	0.006
Age			1.05 (1.02, 1.07)	<0.001
Respiratory rate (breath/min)			1.50 (1.17, 1.94)	0.002
White blood cells (x10^3/µL)			1.21 (1.02, 1.43)	0.032
Aspartate transaminase, AST (U/L)			1.02 (1.01, 1.04)	0.010
Alanine aminotransferase, ALT (U/L)			0.99 (0.98, 1.00)	0.221
Total bilirubin (µmol/L)			1.04 (1.02, 1.06)	0.002
Capillary blood sugar (mmol/L)			1.32 (1.01, 1.73)	0.041
Systolic BP			0.96 (0.94, 0.99)	0.002
Diastolic BP			0.94 (0.91, 0.98)	0.002
Haemoglobin (g/dl)			0.79 (0.63, 0.99)	0.038
Platelet (x10^3/µL)			0.97 (0.96, 0.99)	0.001
Serum bicarbonate (mmol/L)			0.79 (0.69, 0.90)	<0.001

[a] *Likelihood ratio (LR)*

**P values <0.05 are shown in bold.*

JCTN (2021) Volume 1: Article no: 1

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

DISCUSSION

In this cohort of relatively young (mean age 43.5, SD 18), and well (28.3% had at least one underlying medical comorbidity) patients, we noted an incidence of AKI of 31.7%. This is much higher than the 11%-17% as reported in the literature (10,16,17). We postulate several possible explanations.

Firstly, this study, to our knowledge, is one of the few cohort studies on renal outcomes of *P. Knowlesi* infection. It is possible that this species of Plasmodium is more virulent compared to other well studied species, causing more severe infection and organ involvement. More epidemiological studies and research looking into pathophysiology of *P knowlesi* infection are needed to confirm this.

Secondly, the *Sabahan bumiputras* is a group of people that are relatively less studied. It is possible that they may have certain unique biological traits that predispose them to develop AKI in the setting of infections. It is also possible that due to socioeconomic and logistical challenges which are endemic in this cohort, they present themselves relatively later to health facilities when they are unwell, thus increasing the risk of development of organ damage. In our cohort, the patients presented to the health facility after being unwell for a mean of 5.7 days (SD 2.8).

Thirdly, many patients had never had a serum creatinine checked before. The method we employed to diagnose AKI, as described by the ADQI group (13), assumes a normal premorbid renal function in this group of patients, and baseline creatinine is back calculated from GFR of 75ml/min/1.73m2). This method potentially overestimates the incidence of AKI by including patients with undiagnosed CKD in the analysis. A local population based study reported the prevalence of CKD as 9.07%, with only 4% of respondents with CKD being aware of their diagnosis (18).

In this study, through multivariate logistic regression analysis, we noted that the risk of development of AKI is significantly higher among patients who are 50 years old and older (OR 3.25; CI 1.37, 7.73; p=0.008), and high total bilirubin count (OR 5.6; CI 1.73, 18.12, p=0.004). These are important risk factors that have been similarly identified in other similar studies[6,7]. Recognising these risk factors will help identify population at risk of developing AKI, and thus facilitate early implementation of preventive therapy, monitoring and care.

Among the 38 patients who developed AKI due to malaria infection, 5 patients (13%) had persistent deranged renal function at 3 months after discharge. They have stage 3 CKD with eGFR of 44.2 – 51.9ml/min/1.73m^2. This is a large number and is quite alarming.

LIMITATIONS

Despite our best efforts, 53 out of 173 cases of malaria infection were excluded as their case notes were either incomplete or unavailable. This would be a significant source of bias, and highlights the importance of proper filing of case records. To improve the accuracy of reported incidence, we suggest extending this study to involve the whole state of Sabah, either by sampling all diagnosed malaria cases or by random sampling.

All the diagnosis of AKI in this cohort are made based on an increase in serum creatinine from baseline. The urine output of these patients were not meticulously charted, and, as urine output is one of the criteria for the diagnosis of AKI (12), that might have contributed to underestimation of the incidence of AKI. Furthermore, serum creatinine is a late marker of reduction of renal function. Renal damage

Table III: Adjusted Odds Ratio for factors associated with AKI

Parameters	n	% with AKI	Adjusted OR (95% CI OR)	P-value[a]
Age - Less than 50 years old - 50 years and above	 71 49	 21.1 46.9	 1 3.25 (1.37, 7.73)	0.008
Total bilirubin - Normal (≤17.1umol/L) - High (>17.1umol/L)	 33 79	 12.1 40.5	 1 5.60 (1.73, 18.12)	0.004

[a] *Likelihood ratio (LR)*

without overt functional changes would have been missed when diagnosing AKI based on serum creatinine and/or urine output alone (19). The incorporation of novel bio markers in identifying patients with subclinical renal damage is important, as it has been associated with adverse outcomes (20). Incorporating biomarkers to look for kidney injury would likely increase the incidence of AKI.

CONCLUSION

Acute kidney injury is common in malaria due to *Plasmodium* knowlesi infection. 13% of patients with AKI progress to chronic kidney disease at 3 months followup. Further research would be needed to confirm these findings, and if confirmed, would have far reaching implications in the management of malaria and kidney disease.

ACKNOWLEDGEMENTS

The authors would like to thank the Director General of Health Malaysia for permission to publish this paper. We appreciate the invaluable support of Datuk Dr Christina Rundi, Director of Sabah State Health Department and Datuk Dr Heric Corray, Director of Queen Elizabeth Hospital, Kota Kinabalu over the course of this study.

References

1. World Health Organization. World malaria report 2017. Geneva. 2017.
2. William T, Rahman HA, Jelip J, et al. Increasing incidence of *Plasmodium knowlesi* malaria following control of *P. falciparum* and *P. vivax* malaria in Sabah, Malaysia. PLoS Negl Trop Dis. 2013;7:e2026. Doi: 10.1371/journal.pntd.0002026.
3. Barber BE, William T, Grigg MJ, et al. A prospective comparative study of knowlesi, falciparum and vivax malaria in Sabah, Malaysia: High proportion with severe disease from Plasmodium knowlesi and P. vivax but no mortality with early referral and artesunate therapy. Clin Infect Dis. 2013;56:383–97.
4. Mishra SK, Mohanty S, Satpathy SK, et al. Cerebral malaria in adults: A description of 526 cases admitted to Ispat General Hospital in Rourkela, India. Ann Trop Med Parasitol. 2007; 101(3):187–93.
5. Saravu K, Rishikesh K, Parikh CR. Risk Factors and Outcomes Stratified by Severity of Acute Kidney Injury in Malaria. PLoS One. 2014 Mar 13;9(3):e90419. Doi: 10.1371/journal.pone.0090419.
6. Koopmans LC, von Wolfswinkel MEV, Hasselink DA, et al. Acute Kidney Injury in Imported Plasmodium Falciparum Malaria. Malar J. 2015 Dec;14(1):523
7. Saravu K, Rishikesh K, Parikh CR. Risk Factors and Outcomes Stratified by Severity of Acute Kidney Injury in Malaria. PLoS ONE. 2014 Mar; 9(3): e90419. Doi: 10.1371/journal.pone.090419
8. Wailairatana P, Westerlund EK, Aursudkij B, et al. Treatment of malarial acute renal failure by hemodialysis. Am J Trop Med Hyg. 1999;60(2):233-237
9. Rasis WM, Rafidah A, Adlan AMT, et al. A Prospective Study of Acute Kidney Injury in Tropical Acute Febrile Illness in West Pahang, Malaysia. Kidney International Reports. 2017;2(4), S16.
10. Kalaiselvam T, Premila AA, Lim TS, et al. Clinical Outcome of Malaria Cases and Malarial Acute Kidney Injury in Hospital Serdang. A Single Centre Experience from 2007 till 2016. Kidney International Reports. 2017;2(4);S24.
11. Department of Statistics, Malaysia. https://www.dosm.gov.my. Accessed 18 October 2019.
12. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Inter. Suppl. 2012;2:1-138.
13. Bellomo R, Ronco C, Kellum JA, Mehta RL, et al. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care. 2004; 8(4): R204-212
14. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Inter. Suppl. 2013;3:1-150.
15. World Health Organization. Guidelines for the Treatment of Malaria, Third edition. Geneva. 2015.
16. Naqvi R. Plasmodium vivax causing acute kidney injury: A foe less addressed. Pak J Med Sci 2015; 31 (6): 1472-1475
17. Saravu K, Rishikesh K, Parikh CR. Risk Factors and Outcomes Stratified by Severity of Acute Kidney Injury in Malaria. PLoS ONE. 2014 Mar 13;9(3):e90419. doi:10.1371/journal.pone.0090419
18. Hooi LS, Ong LM, Ahmad G, et al. A population based study measuring the prevalence of chronic kidney disease among adults in West Malaysia. Kidney Int. 2013;84(5):1034-40
19. Murray PT, Mehta RL, Shaw A, et al. Potential use of Biomarkers in Acute Kidney Injury: Report and Summary of Recommendations from the 10th Acute Dialysis Quality Initiative Consensus Conference. Kidney Int. 2014 March; 85(3):513-521.
20. Haase M, Devarajan P, Haase-Fielitz A, et al. The Outcome of Neutrophil gelatinase-associated lipocalin-positive subclinical acute kidney injury: a multicenter pooled analysis of prospective studies. J Am Coll Cardiol. 2011 Apr 26;57(17):1752-61

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Case Report

Open Access

THE USAGE OF GUIDEWIRE OR STYLET IN SUCCESSFUL PERITONEAL DIALYSIS CATHETER EXCHANGE WITHOUT FLUOROSCOPY OR PERITONEOSCOPE USE - THE SERDANG METHOD

Azhar Azhani[1], Christopher Thiam Seong Lim[1, 2], Bak Leong Goh[1]

[1] Nephrology Department, Hospital Serdang, Jalan Puchong, 43000 Kajang, Selangor Malaysia.
[2] Unit of Nephrology, Department of Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, 43400 Serdang, Selangor Malaysia.

ABSTRACT

Mechanical malfunction of peritoneal dialysis (PD) catheters remains the most common non-infective complication of peritoneal dialysis. Failure in conservative measures often results in surgical correction, which is often invasive, time-consuming and may require the patient to temporarily switch to haemodialysis while waiting for post-operative recovery and wound healing. This article describes two methods of PD catheter exchange that are minimally invasive, time- and cost-efficient; and most importantly, successful.

Keywords: PD catheter; malfunction; guidewire; stylet

INTRODUCTION

Peritoneal dialysis (PD) catheter is the single most important medical device for patients with end stage kidney disease (ESKD) who choose peritoneal dialysis for long-term renal replacement therapy. Peritoneal dialysis gives ESKD patients the freedom to carry on with their lives independently without causing much disruption. Catheter malposition is one of the most common causes of PD failure, occurring in up to 20% of all catheters (1). Conservative measures to overcome these issues include the usage of laxatives to promote bowel movement, change in body position, saline flushing, increase in physical activity as much as possible have been described, however, the success rate is only about 25 percent (2). If such non-invasive techniques fail, fluoroscopically guided manipulations such as using a rigid cannula, stiff metal rod, tip-deflecting wire, or Lunderquist guidewire may be used to reposition the catheter (3-5).

Failure or unavailability of the methods described above inevitably leads to more invasive surgical revision; either a removal and reinsertion of a new PD catheter, or a laparoscopy-guided insertion. This article describes the exchange of PD catheters using either a guidewire or stylet without fluoroscopy or laparoscopy guidance, which is relatively less invasive, with good post-operative outcome.

FIRST CASE REPORT

A 47-year-old male with a body mass index (BMI) of 22.7 kg/m2 was diagnosed with underlying ESKD secondary to autosomal dominant polycystic kidney disease (ADPKD) in September 2019. Due to his wish to continue working and to minimize disruption to his work, he opted for automated peritoneal dialysis (APD). A PD catheter was successfully placed via peritoneoscope. He completed APD training and continued to self-care with no major issues until six months later when he presented to the PD unit with poor outflow and negative ultrafiltration. A repeat abdominal x-ray (AXR) showed migrated PD catheter tip (figure 1). He was put on interim haemodialysis. Unfortunately, conservative measures failed, and he underwent PD

*Correspondence:
Christopher Lim
Nephrology Unit, Department of Medicine
Faculty of Medicine and Health Sciences,
Universiti Putra Malaysia, 43400 Serdang, Malaysia.
Tel: +6-03-89472568
Email: drchrislim@gmail.com

JCTN (2021) Volume 1: Article no: 2

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

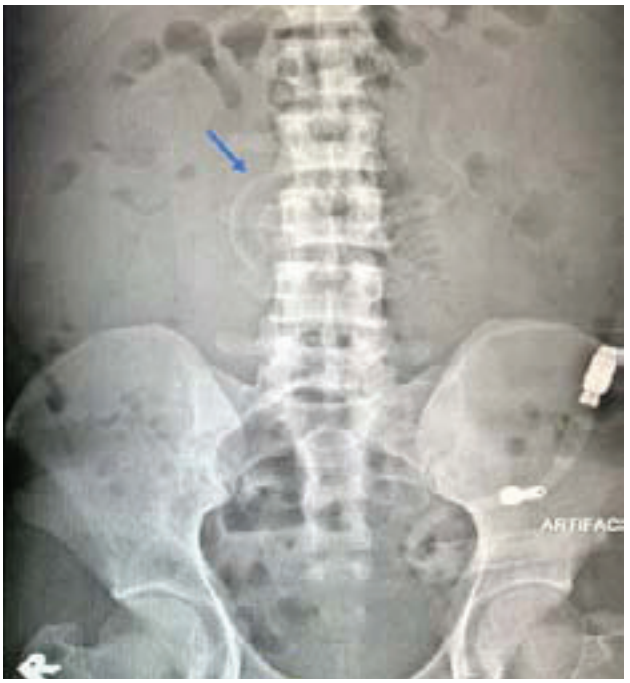


Fig.1: Migrated PD catheter tip.

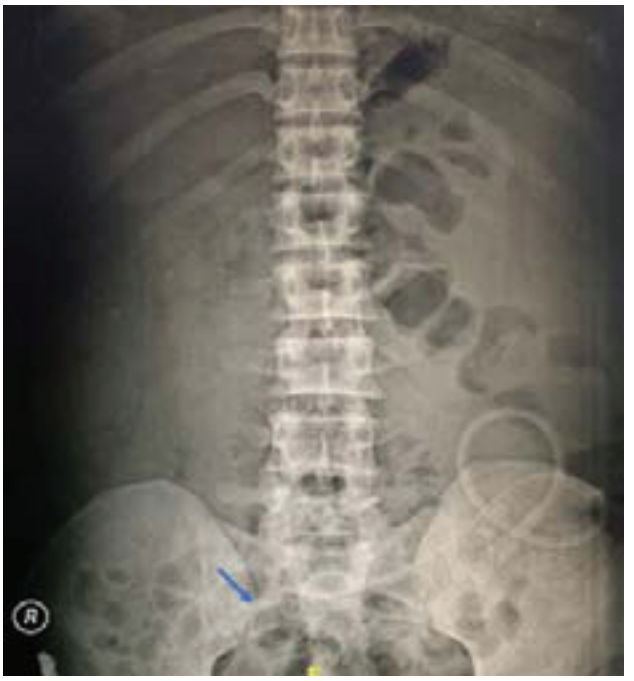


Fig.2: PD catheter post exchange using stylet.

catheter exchange by using a 70-cm stylet (figure 2). After allowing time for post-op healing, he resumed APD 16 days post operation.

SECOND CASE REPORT

The second patient was a 69-year-old male (BMI 31.1 kg/m2) with underlying Type 2 Diabetes, severe ischaemic heart disease (IHD) with 3 vessel involvement based on coronary angiography findings and ESKD for 10 years, previously on haemodialysis. He was converted to APD due to recurrent intradialytic hypotension. He was admitted to our hospital under cardiology unit for acute coronary syndrome (ACS). He was referred to the nephrology team for dialysis support, however APD could not be started due to poor outflow. AXR showed migrated PD catheter. While he was being treated for ACS, he was dialysed via sustained low-efficiency dialysis (SLED). He later underwent PD catheter exchange using a 70-cm guidewire with no complications (figure 3). 2 weeks post operation, he recommenced APD.

THIRD CASE REPORT

A 44-year-old male with BMI of 32kg/m2 on CAPD for 4 months presented to the PD unit complaining of leaking from his PD catheter, approximately 3 cm from the exit site. He denied the usage of any sharp objects while manipulating the catheter. On further inspection, the likely

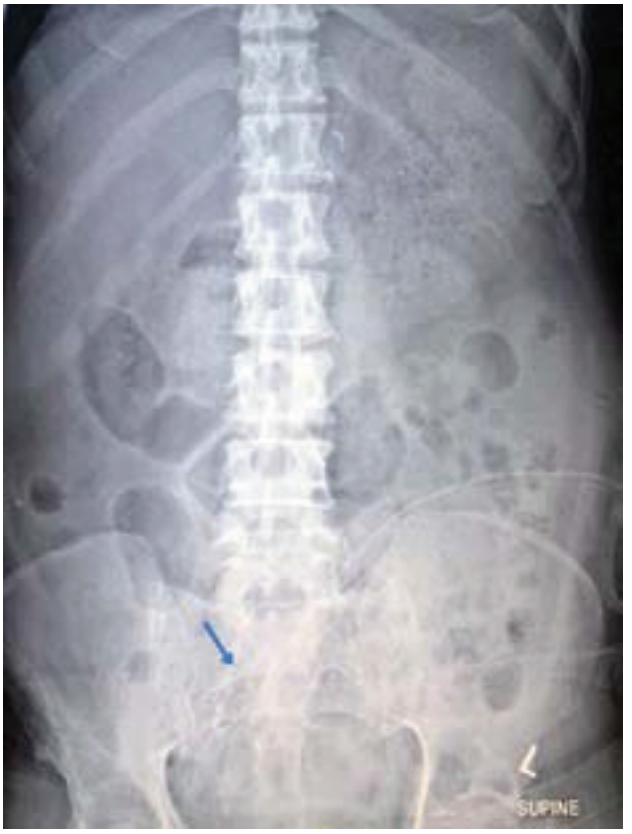


Fig.3: PD catheter post guidewire exchange.

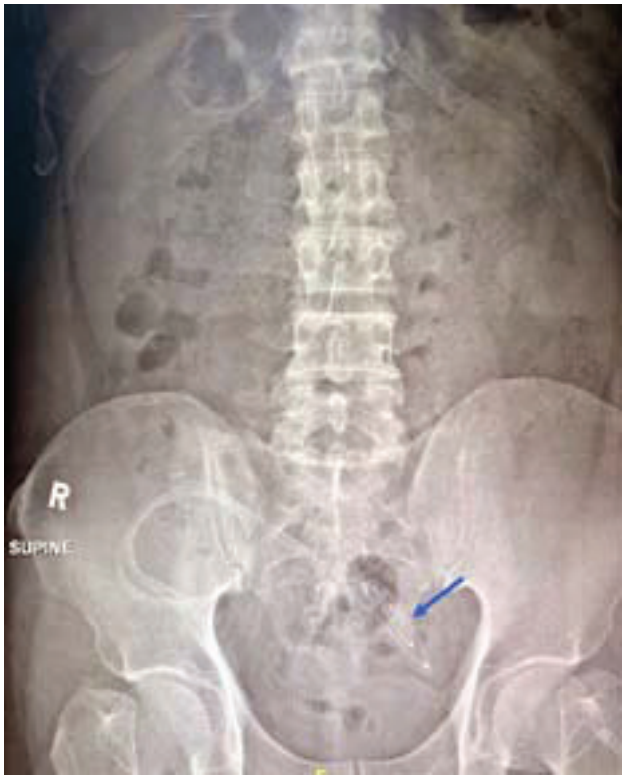


Fig.4: PD catheter post guidewire exchange.

cause of the trauma was due to the pouch zipper used to store the catheter. He was given prophylactic antibiotics and catheter exchange was done under elective OT using a 70-cm guidewire. Figure 4 shows the catheter tip placement post catheter exchange. He had an early break-in period post operatively, resuming with low volume peritoneal dialysis 5 days post operation. He continued his usual CAPD regime after 14 days.

TECHNIQUE DESCRIPTION

All three patients selected for the guidewire/stylet PD catheter exchange procedure had their first catheters inserted via peritoneoscopy, where the peritoneum cavity was visualized prior to insertion to ensure correct placement of the PD catheter. All of them also had used their PD catheters for more than three months before issues arose with their catheter outflow/catheter leak occurred. Patients with concurrent peritonitis were excluded from these exchange methods.

The initial stages of PD catheter exchange procedure were similar for both methods of exchange. The procedures were carried out under strict aseptic conditions in daycare operation theatre on an outpatient basis using sedation and local anaesthesia. Patients were given intravenous midazolam 1-3mg and intravenous fentanyl 20-30mcg (dose adjusted according to patient's sedation level and pain tolerance) prior to sterile preparation and draping of the patient in the operation theatre. Intravenous cefuroxime was administered in each case as antibiotic prophylaxis. Lignocaine 2% was given subcutaneously before incision was made.

During the operation, both the internal and external cuffs of the PD catheters were released. The old PD catheters were cut between the internal and external cuffs to leave a shorter catheter length before threading them through either the stylet or the guidewire. Good inflow and outflow were observed in each of the cases intra-operatively. The duration of each procedure ranged between 20 to 25 minutes for each case from the first incision to the closure of the main wound. There was not immediate complication observed in any of the cases such as bleeding/haematoma, pericatheter leakage or infection, and 3 months post PD catheter exchange all three patients still continued their APD/CAPD without any issues.

1. STYLET METHOD

In the first case, a 70-cm stylet (Figure 5) was inserted through the old PD catheter into the peritoneal cavity before the catheter was removed, leaving the end stylet still within the peritoneal cavity. A new 67-cm double-cuff

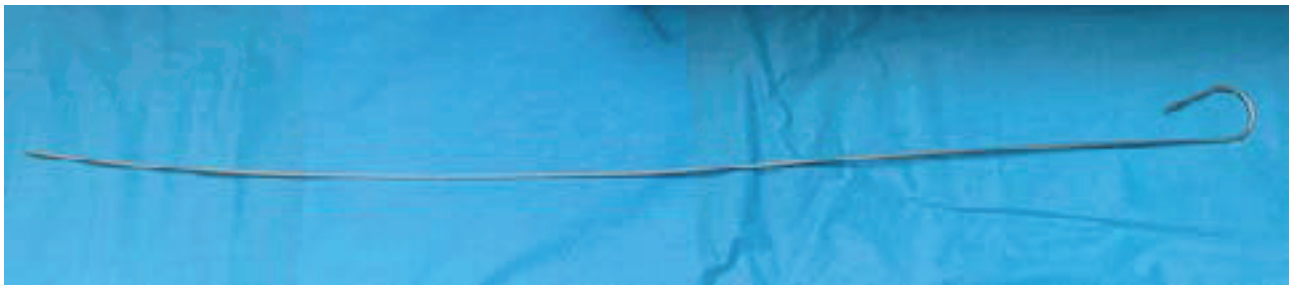


Fig.5: A 70 cm stylet used in the PD catheter exchange. For this purpose, the curved end of the stylet was straightened to ensure ease of threading the new PD catheter through into the peritoneal cavity.

JCTN (2021) Volume 1: Article no: 2

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

PD catheter was then carefully threaded through the stylet (with the curved end straightened) and then placed into the peritoneal cavity (Figures 6a – 6c). The internal cuff of the catheter was then placed within the rectus sheath and the external cuff implanted within the subcutaneous tissue, at least 2 cm away from the new exit site.

2. GUIDE WIRE METHOD

For cases 2 and 3, a 70-cm guidewire was inserted through the old PD catheter before the old catheter was removed (Figure 7a). Subsequent steps were similar to PD catheter insertion via Seldinger method. A dilator and a pull-apart sheath as a single unit were advanced along the guidewire into the peritoneal cavity (Figure 7b). The new PD catheter then was inserted through pull-apart sheath with the guidance of a stylet and placed into its proper position (Figure 7c). The internal cuff was placed just above the anterior rectus sheath and the external cuff implanted within the subcutaneous tissue in the normal fashion.

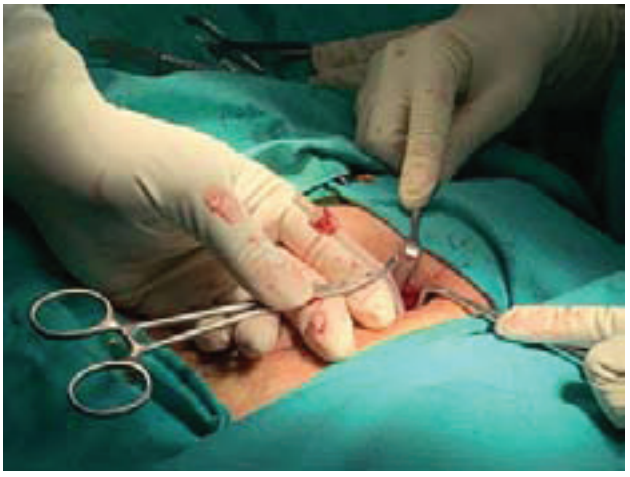


Fig.6a: After releasing both the internal and external cuffs of the catheter, the PD catheter was cut between the internal and external cuff.

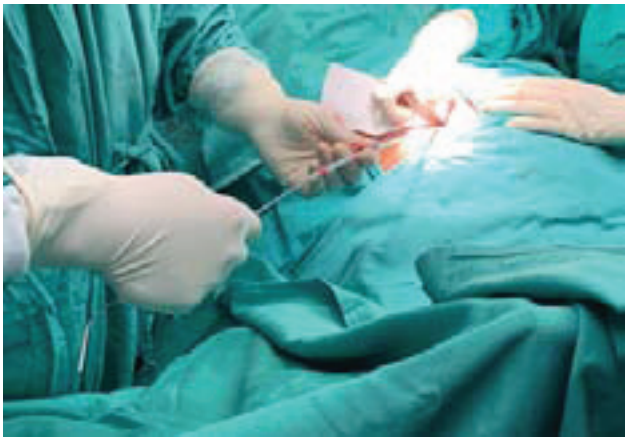


Fig.6b: The 70-cm stylet inserted through the old catheter into the peritoneal cavity and the old catheter removed

DISCUSSION

Peritoneal dialysis is a good option for ESKD patients who are still independent and able to self-care. However, the PD catheter itself remains the Achilles heel of the programme, as the catheter is liable to malfunction which necessitates its exchange or salvage. In the cases described above, two patients underwent PD catheter exchange as the result of catheter malfunction or migration, a common non-infectious complication of PD catheters. The final patient had an exchange due to leaking PD catheter caused by mechanical trauma to the catheter itself, and while the incidence of such cases is not reported, it is not an unheard of occurrence in many PD units, whether accidental or otherwise. The catheter exchanges were done without the use of general anaesthesia or fluoroscopy guidance with good outcome, which is a great advantage to this technique. The perioperative risk involved with the PD catheter exchange using the guidewire or stylet method is not higher compared to the conventional method of PD catheter insertion. The usage of these techniques negated the necessity of another puncture through the intraabdominal wall or creation of a new tract often necessary with new

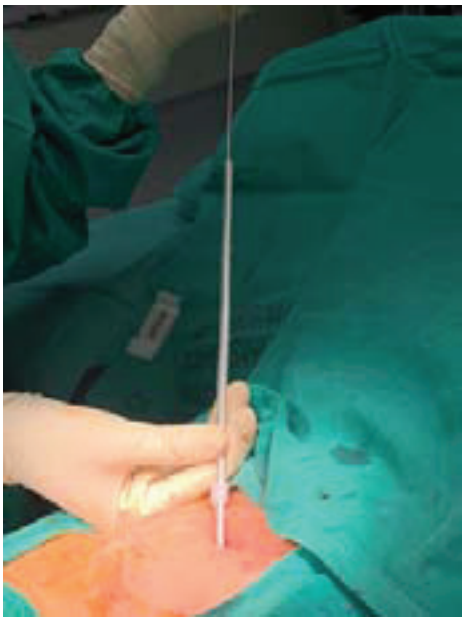


Fig.6c: Insertion of the new PD catheter

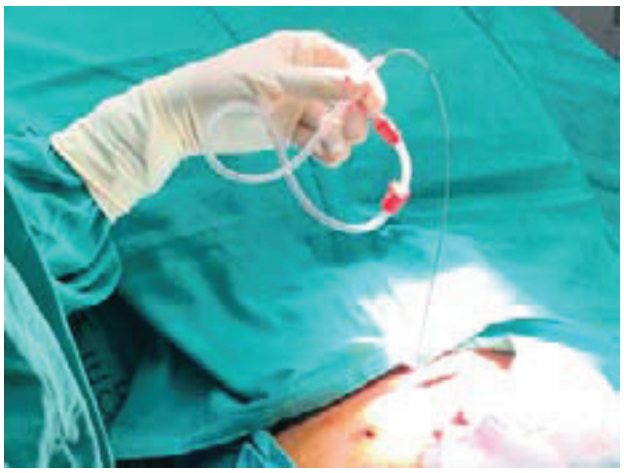


Fig.7a: Removal of the old PD catheter after insertion of guidewire.

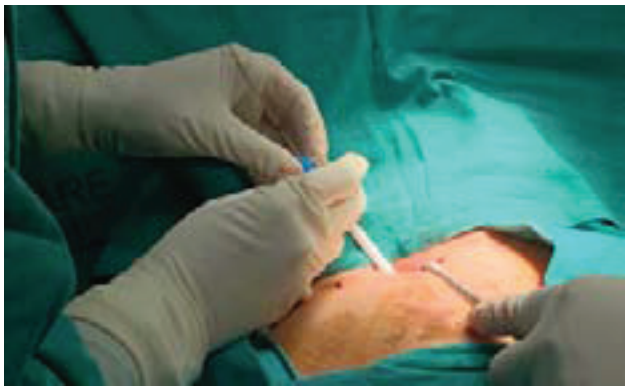


Fig.7b: Placement of dilator and pull-apart sheath into the peritoneal cavity.

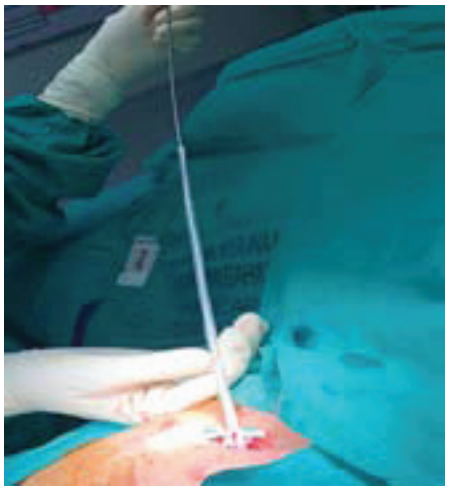


Fig.7c: Placement of the new PD catheter through the pull-apart sheath using stylet as guidance.

catheter insertion, making it less traumatic for the patient while saving operation time and cost. While the articles of other techniques of catheter exchanges (1, 3-5) did not mention the duration of the procedures done for comparison, the operation time of 20 to 25 minutes for the cases in this case report is a short duration of time in itself. However, comparing PD catheter exchange using stylet with guidewire, the guidewire method is relatively more costly as a new Seldinger PD catheter set is required, unlike the stylet method where only a new PD catheter is needed.

The third patient in this case report had early break-in time of the PD catheter by undergoing low-volume intermittent peritoneal dialysis without any leakage issues. This demonstrated that a faster initiating time of PD treatment is possible with the catheter exchange methods useds.

CONCLUSION

PD catheter malfunction is a common occurrence in patients on peritoneal dialysis. First-line management includes conservative manoeuvres such as laxatives, saline flushing and change in body position. Failure to manage the issue conservatively leads to surgical management. PD catheter exchange using guidewire or stylet as described in this article have demonstrated two different techniques which are successful, minimally invasive, and less traumatic to the patient.

References

1. Jones B, McLaughlin K, Mactier RA, Porteous C. Tenckhoff catheter salvage by closed stiff-wire manipulation without fluoroscopic control. Peritoneal dialysis international. 1998 Jul;18(4):415-8.
2. Ogunc G. Malfunctioning Peritoneal Dialysis Catheter and Treatment. http://www.smgebooks.com/Progress-in-Peritoneal-Dialysis/chapters/PPD-16-02.pdf. Accessed 5 November 2020.
3. Lee CM, Ko SF, Chen HC, Leung TK. Double guidewire method: a novel technique for correction of migrated Tenckhoff peritoneal dialysis catheter. Peritoneal dialysis international. 2003 Nov;23(6):587-90.
4. Moss JS, Minda SA, Newman GE, Dunnick NR, Vernon WB, Schwab SJ. Malpositioned peritoneal dialysis catheters: a critical reappraisal of correction by stiff-wire manipulation. American Journal of Kidney Diseases. 1990 Apr 1;15(4):305-8.
5. Jwo SC, Chen KS, Lee CM, Huang CY. Correction of migrated peritoneal dialysis catheters using Lunderquist guidewire: a preliminary report. Peritoneal dialysis international. 2001 Nov;21(6):621-3.

JCTN (2021) Volume 1: Article no: 3

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Case Report

Open Access

ACUTE BILATERAL BASAL GANGLIA LESION: LENTIFORM FORK SIGN IN END STAGE KIDNEY DISEASE WITH METABOLIC ACIDOSIS

Lau Siew Ping
Department of Nephrology, Selayang Hospital, 68100 Batu Caves, Selangor, Malaysia

ABSTRACT

Neurological complications are not uncommon in end stage kidney disease population. Bilateral basal ganglia lesions have been frequently reported in patients with uraemic encephalopathy or metabolic acidosis. Lentiform Fork sign is a distinctive, as described in MRI picture that is not only seen in patient with uraemic encephalopathy, but also in other condition that presented with metabolic acidosis.

Keywords: bilateral basal ganglia lesion. Metabolic acidosis.

INTRODUCTION

Bilateral basal ganglia lesions have been described in end stage kidney patients, especially those who have diabetes or metabolic acidosis (1). The vulnerability of basal ganglia to metabolic acidosis and ureamic encephalopathy is well described in several case reports and literature reviews.

CASE REPORT

A 46-year-old Malay woman who had been receiving haemodialysis three times per week for past thirteen years was found lethargy, generalised weakness, slow response, and slurred speech, and respiratory distress. Additionally, she had missed her one haemodialysis session before presented to emergency department. On neurologic evaluation, the patient scored E3V4M6 on the Glasgow Coma Scores (GCS). The patient's medical history was notable only for end stage kidney disease with unknown primary disease and hypertension.

The patient's laboratory investigation results were shown in Table 1 with predominantly metabolic acidosis with lactic acidosis. Computed tomography (CT) brain on arrival showed hypodensities at both basal ganglia with no focus focal haemorrhage. The patient was treated with sustained low efficiency dialysis (SLED) and supportive care that led to improvement in blood chemistry. She was able to wean off mechanical ventilation on day 2 of admission. However, the patient's GCS scored E2V2M5on Day-4 and reintubated for airway protection. Repeated CT brain (Figure A) showed worsening bilateral basal ganglia hypodensities with effacement of the adjacent cerebral sulci. Magnetic resonance imaging (MRI) of the brain was done showed hyperintensity regions bilaterally in the basal ganglia surrounded by more hyperintense rim, suggestive of lentiform fork sign (Figure B).

We presumed that the new deterioration of her GCS was due to metabolic acidosis in origin given their radiological correlation, and continuous renal replacement therapy was commenced for her cerebral protection and intermittent intravenous mannitol was given for her cerebral edema.

*Correspondence: Lau Siew Ping
Department of Nephrology
Lebuhraya Selayang - Kepong,
68100 Batu Caves, Selangor
Malaysia
Email: siewpinglau@gmail.com

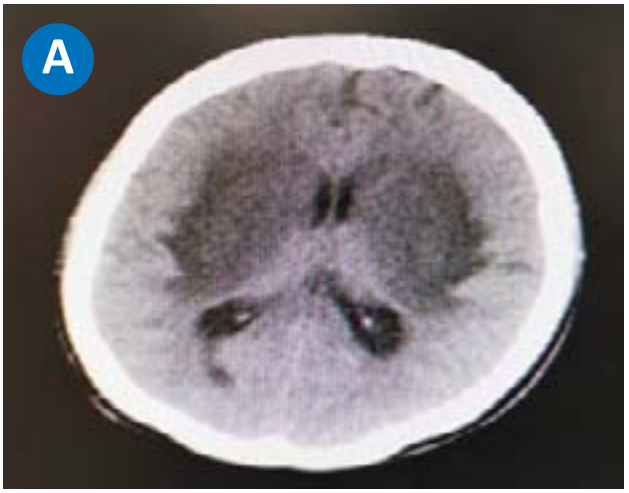
JCTN (2021) Volume 1: Article no: 3

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

Table 1 showed the patient's investigation results:

Test		***Reference range***
Haemoglobulin	10.2	*12 - 15 g/dL*
Total white cell	9.07	*4 – 10 x 109/L*
platelet	299	*150 - 410 x 109 /L*
prothrombin	16.2	*11.6 – 14.1 sec*
aPTT	33.9	*31.4 – 43.3 sec*
Sodium	135	*135 – 150 mmol/L*
Potassium	4.7	*3.5 – 5.0 mmol/l*
Urea	18.9	*1.7 – 8.3 mmol/l*
Albumin	41	*35 – 50 g/L*
Random blood glucose	5.2	
Calcium	2.47	*2.10 – 2.60 mmol/l*
Phosphate	2.23	*0.80 – 1.45 mmol/l*
CRP	0.96	*< 0.80 mg/dL*
pH	6.976	*7.35 – 7.45*
PaO2	295	*75 – 100 mmHg*
PaCO2	31.6	*38 – 42 mmHg*
HCO3	7.9	*22 – 26 mmol/l*
Base excess	-20.7	*-3.0 – 3.0 mmol/l*
Lactate	15	*0.5 – 1 mmol/l*



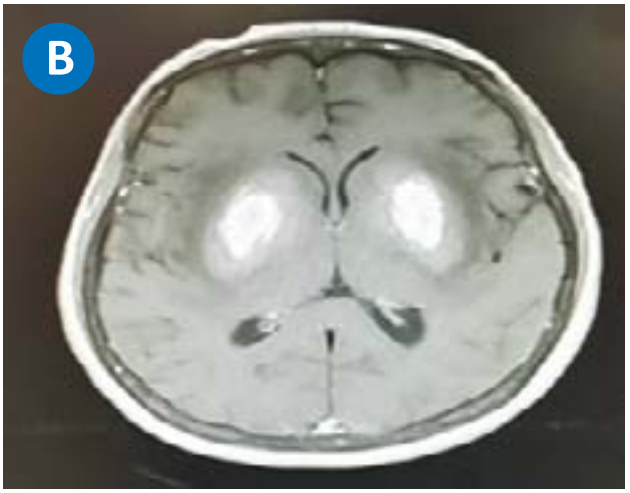


Figure A CT brain contrast revealed worsening bilateral basal ganglia hypodensities with involvement of the adjacent white matter and thalami. There was effacement of the adjacent cerebral sulci, frontal horns of both lateral ventricles and third ventricles. Figure B MRI of the brain (non-contrast) showed both globus pallidus demonstrated heterogenous hyper and hypointensity, involving of both putamina in lesser extends. Heterogenous avid enhancement of both globus pallidus and the peripheral enhancement in T2-weighted MRI

JCTN (2021) Volume 1: Article no: 3

JOURNAL OF CLINICAL AND TRANSLATIONAL NEPHROLOGY (JCTN)

Open Access

2 weeks later, her GCS improved with E4VTM6 and repeated CT brain showed lesser degree of cerebral edema. However, her condition was complicated with ventilated associated pneumonia due to prolonged ventilation. The patient was succumbed on day-18 of hospitalization.

DISCUSSION

Bilateral basal ganglia lesions have been well described in end stage renal disease patients, commonly presented in patients with diabetes mellitus and metabolic acidosis. The clinical presentation is usually acute onset, which involved neurological disorders like drowsy or movement disorder. Lentiform fork sign has been described as a distinctive radiological finding in end stage kidney disease (ESKD) with uraemic encephalopathy or metabolic acidosis, which may suggest metabolic cause or metabolic acidosis can be an important aspect in the pathogenesis (3).

In literature review, 90% of patients at presentation had associated with metabolic acidosis (4). The most interesting character of this syndrome is the consistency of the neuroimaging finding with CT brain uniformity revealed bilateral hypodense basal ganglia lesion and MRI brain showed bilateral hypointense area in the basal ganglia on T1-weighted images and hyperintense area on T2-weighted images (1-5).

The exact pathogenesis of appearance of Lentiform fork sign in ESKD is still in mystery. Metabolic acidosis possible increases susceptibility basal ganglia to insults, and high frequency of the co-existing diabetes may further increase the risk. In Gyanendra review, several of the acidotic condition related to the Lentiform Fork sign, are well known associated with increased cerebral lactate production. As an ultimate common pathway, through the changes in vascular reactivity, metabolic acidosis may disrupt the brain blood barrier leading to vasogenic edema and later cytotoxic edema, proportionate the severity of acidosis on presentation. In this case report, the clinical course is acute onset but reversible with the resolution of metabolic acidosis and cerebral edema.

The main treatment for this presentation included correction of uremia and metabolic acidosis as supportive therapy, and prevention of worsening of cerebral edema has been the focus of management. Mode of renal replacement therapy depend on the severity of cerebral edema of the patient. The neurological symptoms usually improved gradually: 20% showed complete resolution, 30% showed no neurological improvement and the rest showed partial recovery. Neurological and clinical improvement do not correlate with severity of radiographically changes (4).

CONCLUSION

Lentiform fork sign is an important radiological finding to differentiate the important aetiology from other conventionally causes for basal ganglia lesions. Metabolic acidosis in ESKD patients with radiological finding of lentiform fork sign can help to exclude other long list causes of bilateral ganglia lesions.

Conflict of interest: There is no conflicts of interest to declare.

Consent to participate: The author declares the next of kin of the patient provided authorities for use of her medical records as research.

References

1. Kumar G, Goyal MK (2010) Lentiform fork sign: a unique MRI picture. Is metabolic acidosis responsible? Clin Neurol Neurosurg 112(9):805–812. doi:10.1016/j.clineuro.2010.06.006
2. Fabiani G, Teive HA, Munhoz RP (2013) Lentiform fork sign and fluctuating, reversible parkinsonism in a patient with uremic encephalopathy. Movement Disorder 28(8):1053. doi:10.1002/mds.25503
3. Manish R, Chetan M. Lentiform fork sign in a case of end-stage renal disease. Kidney International (2012) 82, 365; doi:10.1038/ki.2012.119
4. Li JY, Yong TY, Sebben R, Khoo E, Disney AP (2008) Bilateral basal ganglia lesions in patients with end-stage diabetic nephropathy. Nephrology (Carlton) 13(1):68–72. doi:10.1111/j.1440-1797. 2007.00838.x
5. Jaryal A, Thakur S. Lentiform fork sign: Uraemia alone or multifactorial causation? Haemodialysis International 2020: 24: E10-E12. DOI:10.1111/hdi.12810