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Microbiology, Clinical Profile and Outcomes of Continuous Ambulatory Peritoneal Dialysis associated Peritonitis

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ABSTRACT

Introduction

CAPD associated peritonitis is a common complication associated with high morbidity and mortality. Clinical data regarding peritonitis is scarce in our population. In this study, we aimed to determine the microbiology, clinical profile and outcomes of peritonitis in CAPD patients at a tertiary referral center in Nepal.

Methods

A retrospective, observational study was conducted at a tertiary care center in Kathmandu over a period of two years from August, 2022 to July 2024. Data on demographics, clinical presentation, organisms isolated, treatment and outcomes were retrieved. Statistical analysis was done by using SPSS v26. The categorical data and continuous data were analyzed using mean, standard deviation and percentage.

Results

There were 20 episodes of peritonitis in 17 patients. There were eight male patients. Mean age of the patients was 48.45± 9.6 years. Sixteen were culture positive (80%). Peritonitis due to gram-negative organisms 10 (62.5%) was higher. The most common organisms isolated were *Pseudomonas aeruginosa* (4) followed by *Escherichia coli* (2), *Klebsiella* sp. (2), *Staphylococcus aureues* (2), coagulase negative *Staphylococcus* (2) and *Enterococcus* sp. (2). The most common clinical presentation was abdominal pain. Fifteen percent episodes were constituted by refractory, recurrent and repeat peritonitis. Outcomes were recovery (95%), catheter removal and switch to hemodialysis (5%). There were no deaths due to peritonitis in the study population.

Conclusion

CAPD peritonitis due to Gram-negative organisms was more frequent than that due to gram-positive organisms in our CAPD population. Most of the patients of CAPD recovered.

Keywords
CAPD; continuous ambulatory; microbiology; outcome; peritonitis

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INTRODUCTION

Chronic kidney disease (CKD) in Nepal has a reported population prevalence of 6%.[1] Continuous ambulatory peritoneal dialysis (CAPD) has become an increasingly popular mode of treatment of patients with end-stage kidney disease (ESKD) with up to 29% of them being on CAPD.[2] However, the greatest limiting factor for the expansion of CAPD is peritoneal dialysis (PD)-related infections, especially peritonitis, either alone or in combination with exit-site and tunnel infections.[3]

Peritonitis is the most common cause of technique failure and leads to significant morbidity and mortality of up to 18%.[4] The rate of peritonitis is variable between centers, even in the same country.[5] Microbiological spectrum of CAPD peritonitis in developing countries such as Nepal may be different from that in developed countries and this may be due to the differences in environmental, social, educational and economic background of the patients on PD.[6] International Society for PD (ISPD) guidelines state that antibiotic treatment must be adjusted based on the microscopy or culture results after the initial empiric therapy for CAPD peritonitis.[4] Isolation and identification of the causative organism to prevent unnecessary broad-spectrum antibiotic exposure, continues to be a diagnostic challenge. Several methods are used to improve the sensitivity of culturing peritoneal dialysate including automated culture techniques, centrifugation, enrichment, large volume culture, filtration and cell lysis.[7]

Data on CAPD-associated peritonitis in Nepalese population is limited. Therefore, this study was planned to determine the microbiology, clinical profile and outcomes of peritonitis in CAPD patients.

METHODS

This was a retrospective, observational, cross sectional study conducted over a period of two years in Tribhuvan University Teaching Hospital (TUTH), a tertiary care teaching hospital in Kathmandu, Nepal. All adult patients aged 18 years or older admitted with confirmed or presumed diagnosis of CAPD-peritonitis between August 1, 2022 and July 31, 2024 were included in the study. Patients aged <18 years and those with missing data were excluded.

Anonymous data were collected from the hospital records after approval from the Department of Nephrology and Transplantation Medicine and ethical clearance from Institutional Review committee (IRC. Reference Number:238 (6-11) E2 081/082.) The patient consent was not applicable as this was a retrospective study which involved collection of anonymous data from past hospital records. Detailed history was recorded in the proforma which included demographic and clinical characteristics, aetiology of ESRD, presence of comorbidities, previous peritonitis episodes, and the time to current peritonitis episode. Data regarding organisms isolated in culture, their susceptibility to antibiotics, duration of antibiotic use, treatment response and outcomes were retrieved from hospital records. The outcomes were analysed as recovery, catheter loss, switch to hemodialysis and death within 4 weeks of peritonitis.

Operational Defintions

Peritonitis, repeat, relapse, recurrent and refractory peritonitis were defined according to the ISPD criteria as detailed below.[4]

- CAPD-associated peritonitis: Diagnosed when at least 2 of the following were present:
  - Clinical features consistent with peritonitis i.e. abdominal pain and/or cloudy peritoneal dialysis effluent
  - Peritoneal dialysis effluent white cell count >100/microliter (after a dwell time of at least 2 hours) with >50% polymorphonuclear leukocytes
  - Positive peritoneal dialysis effluent cultures
- Refractory Peritonitis: Defined as failure of the peritoneal effluent to clear after 5 days of appropriate antibiotics.
- Recurrent Peritonitis: An episode of peritonitis that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism.
- Relapsing Peritonitis: An episode of peritonitis that occurs within 4 weeks of completion of therapy of a prior episode with the same organism.
- Repeat Peritonitis: An episode of peritonitis that occurs more than 4 weeks after completion of therapy of a prior episode with the same organism.

Peritoneal dialysis catheter insertion and Patient education

Peritoneal dialysis catheters were kept by surgeons as there was lack of training to nephrologists at the study center during the study period. Proper education and counselling regarding PD care including hand hygiene; symptoms suggestive of peritoneal dialysis associated peritonitis and when to consult nephrologists was given to the patients as well as their care-givers before, during and after initiation of PD.

Sample processing

The patients' exchange bags containing effluent dialysate were transported to the microbiology laboratory for culture on the same day of collection. The bags not processed immediately, were

refrigerated at 4°C. From these exchange bags, 100 ml of fluid was withdrawn with a sterile needle and syringe under aseptic conditions. This fluid was centrifuged in sterile tubes at a rate of 3000 g for 15 minutes and supernatant was discarded, leaving 0.5 ml of deposit. In the centrifuged deposit, 10 ml of sterile distilled water was added and the mixture was shaken vigorously for 30 seconds. After vigorous shaking, the deposit was centrifuged at 3,000 g for 15 min and supernatant was discarded. The deposit was divided into three parts, the first part of the deposit was used for gram staining, Ziehl-Neelsen (ZN) staining, and 10% KOH mount to detect the presence of yeast cells or fungal hyphae.

The second part of the deposit was used for culturing the bacteria which was done on Blood agar (BA) and MacConkey agar at a temperature of 37°C for 24-48 h. Culturing for fungi was done on Sabouraud-Dextrose agar with and without antibiotics at temperatures of 25°C and 37°C for 4 weeks, and culturing for mycobacteria was done on Lowenstein Jensen medium at 37°C for 8-12 weeks.

The third part of the deposit was inoculated into Brain-Heart Infusion (BHI) broth and incubated at 37°C. BHI broth was observed daily for the development of turbidity. After the development of turbidity, the fluid was gram-stained and plated on appropriate media for isolation and identification of the microorganisms. BHI broths showing no growth were discarded after seven days of incubation.

The drug sensitivity was done by Kirby-Bauer disc diffusion method on Mueller Hinton agar. For gram-positive organisms, ampicillin, amoxiclavulanic acid, cefazolin, clindamycin, and vancomycin discs were tested. The cefoxitin discs were used to detect methicillin-resistant Staphylococcus aureus (MRSA). For gram-negative organisms, ciprofloxacin, cefotaxime, ceftriaxone, ceftazidime, cefepime, gentamicin, piperacillin– tazobactam, imipenem and meropenem discs were tested as per Clinical and Laboratory Standard Institute guidelines for antimicrobial susceptibility testing.

The total and differential count as well as culture was repeated after 5 days of treatment to see the treatment response.

Data Analysis

Data were analyzed with IBM SPSS Statistics version 26 software which was available as a 14-day free trial at the time of data analysis. The categorical data were analyzed by using the Chi-square test and represented as frequency in tables, pie charts and bar diagrams. Continuous data were analysed using the Student's t-test and represented as mean or median. $P < 0.05$ was considered statistically significant.

RESULTS

Mean age of the patients was 48.45 ± 9.6 years and the age range was 35-76 years. There were 8 male and 9 female patients.

Causes of ESRD

The causes of ESRD are shown in Figure 1.

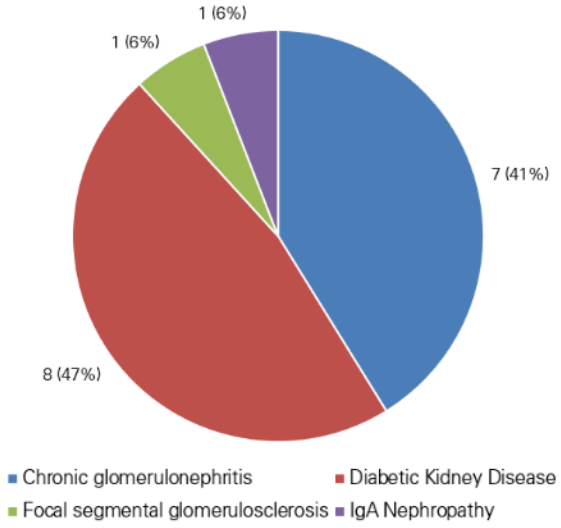


Figure 1. *Causes of ESRD in the study population*

Co-morbidities

The associated co-morbidities in the study population were as shown in Table 1.

Table 1. *Associated co-morbidities in the study population*

Co-morbidities	Frequency	Percentage
Hypertension	15	88.24
Diabetes mellitus	9	50.94
Coronary artery disease	1	5.88
Stroke	1	5.88
Peripheral artery disease	1	5.88
Hypothyroidism	1	5.88

Presenting symptoms and signs

There were 20 episodes of CAPD-associated peritonitis in 17 patients. Table 2 shows presenting symptoms and signs of patients with CAPD peritonitis.

The most common presenting symptoms were abdominal pain in 17 (85%) and cloudy peritoneal effluent 14 (70%). Most common signs were abdominal tenderness 17 (85%) and cloudy peritoneal effluent 14 (70%).

Table 2. *Presenting symptoms and signs in the study population (N=20)*

Presenting Symptoms and Signs	Frequency	Percentage
Symptoms		
Abdominal pain	17	85
Cloudy peritoneal effluent	14	70
Vomiting	10	50
Anorexia	10	50
Limb swelling	8	40
Nausea	7	35
Fever	5	25
Diarrhea	4	20
Shortness of breath	3	15
Signs		
Abdominal tenderness	17	85
Cloudy Peritoneal Effluent	14	70
Pallor	12	60
Edema	9	45

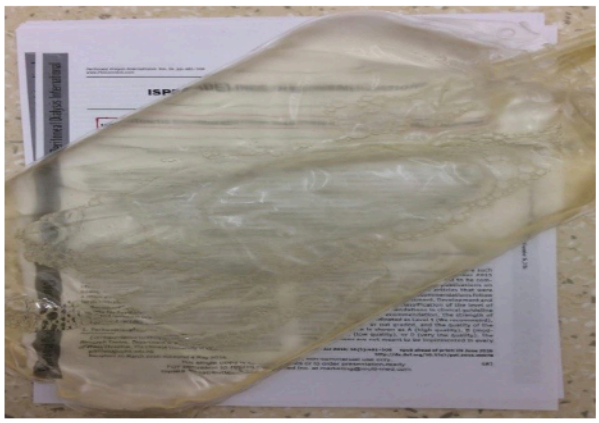


Figure 2. *Clear peritoneal effluent*

Figure 3. *Cloudy peritoneal effluent*

Laboratory parameters

The most common laboratory abnormalities in the study population are shown in the Table 3.

Table 3. *Laboratory parameters in the study population*

Laboratory Parameter	Minimum value	Maximum value	Mean Value ± SD
Hemoglobin (g/dl)	3.8	14.4	9.01 ± 2.49
Total leukocyte count (per mm^3)	2900	12400	7509 ± 2092
Platelet count (x 103 per mm^3)	70	502	188.53 ± 111.56
Urea (mmol/l)	11.7	39.0	21.54 ± 8.37
Creatinine (µmol/l)	420	1588	852.10 ± 266.10
Sodium (mEq/l)	129	138	132.85 ± 2.61
Potassium (mEq/l)	3.5	5.6	4.48 ± 0.62
Initial peritoneal dialysate TLC (per mm^3)	300	9400	2575 ± 2257
Initial Peritoneal dialysate ANC (per mm^3)	210	7520	2016 ± 1807
Repeat Peritoneal dialysate TLC (per mm^3)	10	17600	291 ± 334
Repeat Peritoneal dialysate ANC (per mm^3)	0	1264	88 ± 130

Abbreviations: ANC: Absolute neutrophil count, PD: Peritoneal Dilaysis, TLC: Total leukocyte count, mEq/L: milliequivalent/liter, mmol/l: millimoles/liter, mm: millimeter, µmol/l: micromoles/liter

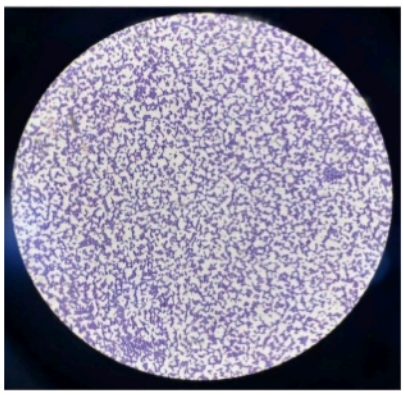
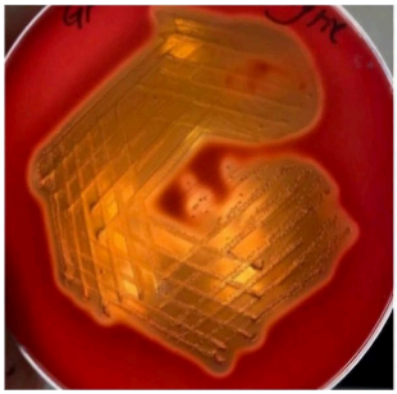


Figure 4. *Gram stain showing Gram positive cocci in bunches (Staphylococcus aureus)*



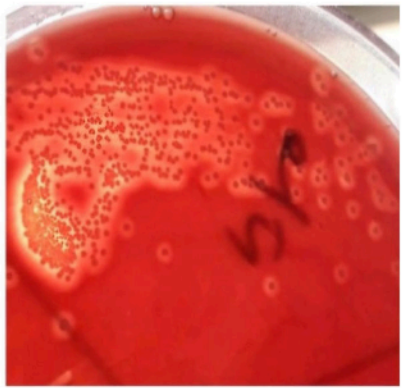


Figure 5. *Isolates of Staphylococcus aureus showing beta hemolytic colony blood agar*

Microbiological culture and sensitivity

Among 20 episodes of PD infections, 16 episodes were culture positive and 4 episodes were culture negative giving a culture negative rate of 20%. Peritonitis due to Gram-negative organisms was seen in 10 episodes while peritonitis due to Gram-positive peritonitis was seen in 6 episodes.

The most common organism isolated was Pseudomonas aeruginosa. The most common clinical presentations were abdominal pain and cloudy peritoneal effluent. 15% episodes were refractory, recurrent and repeat peritonitis.

The mean duration of CAPD was 12.6± 4.1 months and the range of CAPD duration was (3-132) months. Fungal KOH & C/S were negative in all 20 (100%) cases. Similarly, acid fast bacilli (AFB) were negative in all 20 (100%) cases.

Table 4. *Organisms isolated in the study population*

Organisms isolated	Frequency	Percentage
Organisms isolated	6	30
Staphylococcus aureus	2	10
Coagulase negative Staphylococcus	2	10
Enterococcus	2	10
Gram negative bacilli	10	50
Pseudomonas	4	20
Klebsiella	2	10
Escherichia coli	2	10
Citrobacter	1	5
Acinetobacter	1	5

Organisms isolated

The organisms isolated in culture are shown in the Table 4.

Episode and type of peritonitis

The episode and type of peritonitis is shown in table 5.

Table 5. *Episode and type of peritonitis*

Episode and type of peritonitis	Frequency	Percentage
Episode of peritonitis		
First	17	85
Second	2	10
Third	1	5
Type of Peritonitis		
First episode	17	85
Refractory	1	5
Recurrent	1	5
Repeat	1	5

Treatment of CAPD associated peritonitis

Empirical treatment

Our institutional protocol for treatment of CAPD associated peritonitis is intraperitoneal (IP) ceftazidime + intraperitoneal (IP) vancomycin. All 20 (100%) episodes received intraperitoneal (IP) ceftazidime + intraperitoneal (IP) vancomycin for empirical treatment of CAPD-associated peritonitis.

Definitive treatment

The definitive treatment after the availability of

culture and sensitivity (C&S) report was same as empirical treatment in 15 (75%) episodes. The treatment was changed to piperacillin-tazobactum, meropenem or gentamicin in 5 (25%) episodes after Culture and sensitivity report. Intravenous (IV) treatment was required in 5 (25%) episodes. The mean duration of hospitalization was 6 ±1.6 days and the range was (4-31) days. Mean duration of antibiotics used was 16.8 ± 3.43 days and the range was 14-21 days. Mean duration of hospitalization was 12.55 ± 7.15 days.

Outcome of CAPD associated peritonitis:

The outcome of CAPD associated peritonitis is shown in Table 6.

Table 6. *Outcome of CAPD associated peritonitis*

Outcome	Frequency	Percentage
Recovery	19	95
PD catheter removal and switch to HD	1	5
Re-implantation of catheter	0	0
Death	0	0

DISCUSSION

Peritonitis is the major Achilles heel of CAPD programme leading to high morbidity, mortality and technique failure. Many centers have reported peritonitis in CAPD patients with varying rates of culture positivity. In our study, 17 patients had 20 episodes of CAPD-associated peritonitis. Most common age group for CAPD-associated peritonitis was 31-50 years followed by 51-70 years with the mean age being 48.45± 9.6 years which is similar to other studies from India.[5,8]

ESRD was due to diabetic nephropathy (45%) and chronic glomerulonephritis (45%) in most of the patients which was similar to other studies from Nepal and India. In a study by Pindi et al in India, diabetes (41.3%) and hypertension (32%) were the most common cause of ESRD.[8] In a study by Sharma et al in Eastern Nepal, diabetes mellitus (62%) and hypertension (24%) were the most common cause of ESRD whereas in another study by Maskey et al in Western Nepal, diabetes mellitus (31%) and hypertension (25%) were the most common cause of ESRD.[9,10] Diabetes is not only the cause for ESRD, but also an independent risk factor for peritonitis.[6] It leads to a faster decline of renal function.[11]

In our study, all patients had one or more non-renal co-morbidity. Half of the patients had single co-morbidity as hypertension. A quarter had two co-morbidities while another quarter had more than two co-morbidities. All patients with DM were associated with at least one other co-morbidity. Similar results were seen in other studies from India and Nepal.[8,12] In a study by Pindi et al in India 96% patients had one or more non-renal co-morbidity and 68% patients had two or more comorbidities.[8] In a study by Sharma et al in Nepal 76% patients had one or more non-renal comorbidity.[9] Similarly, in another study by Vikrant et al in India 100% patients had one or more non-renal co-morbidity and 62% patients had two or more comorbidities.[12]

Abdominal pain (85%) and cloudy PD bag (70%) were the most common symptoms. Similar results were seen in other studies from India and Western countries. In a study by Pindi et al abdominal pain (94%) and cloudy PD bag (94%) were the most common symptoms.[8] Costa et al also found that abdominal pain (93%) and cloudy peritoneal effluent (95%) were the most common symptoms.[5]

The International Society of Peritoneal Dialysis (ISPD) guidelines recommend that culture negativity should not be more than 20%.[4] Culture negativity (20%) in our study was as per ISPD recommendation and also similar to other studies from India and Nepal. In a study by Pindi et al, culture negative peritonitis was 13% whereas in a study by Maskey et al culture negativity was 16.67%.[8,10] The earlier study done by Sharma et al, culture negativity was 46%.[9] Prasad et al reported that their culture negativity reduced from 36.9% in 2003 to 18.2% in 2014 after improvement in microbiological culture technique.[13]

Worldwide, the most common cause of peritonitis are gram-positive cocci followed by gram-negative bacilli. However, our study found gram-negative bacilli (50%) followed by gram-positive cocci (30%) as the most common cause of peritonitis. This differs from the studies from Western countries where gram positive cocci are the main causes of CAPD-associated peritonitis. However, published reports from India showed that gram-negative pathogens account for 60-65% of all positive cultures.[14]

CAPD-associated peritonitis could be caused by touch contamination, catheter-related problems, bowel pathology, gynaecological disease or systemic bacteremia. In a study done by Gadola et al, peritonitis caused by gram-negative microorganisms was more severe and was associated with significantly higher adverse outcomes including mortality whereas peritonitis caused by gram-positive organisms was less severe and usually responsive to intraperitoneal antibiotic treatment at home.[15] Improved connection technology eliminating spike systems and using Y systems and flush before fill technique, Staphylococcus aureus prophylaxis with mupirocin ointment and the use

of new, more biocompatible dialysis solutions may account for reduction in gram-positive peritonitis. Despite advances in PD system connectology, contamination at the time of PD exchange is still a major cause of peritonits. Our study involved patients who were hospitalized for the treatment of CAPD-associated peritonitis which are reported in the literature to be more severe and caused by gram-negative micro-organisms. These multiple factors may be responsible for reduction in gram-positive peritonitis in our study population.

Gram positive organisms were responsible for 37.5% culture-positive episodes of peritonitis. Among gram-positive organisms, Staphylococcus aureus (2), CoNS (2) and Enterococcus (2) accounted for 6 episodes of CAPD-associated peritonitis.

Gram-negative organisms were responsible for 62.5% of culture-positive peritonitis. Among gram-negative organisms, Pseudomonas aeruginosa (4), Escherechia coli (2) and Klebsiella pneumonia (2) were the most common cause of gram negative peritonitis. Lin et al and Pindi et al described very high incidence of gram-negative peritonitis due to Klebsiella and these patients had higher incidence of sepsis or bacteremia and mortality.17 Acinetobacter (1) and Citrobacter (1) were other causes of gram negative peritonitis.

In recent years, fungal peritonitis is increasingly recognized with an incidence of 1-15% in various studies.18 In a study by Pindi et al rate of fungal peritonitis was 6.89% of total culture –positive episodes.[8] Similarly, in a study by Maskey et al 6% of total culture-positive episodes were due to fungi.[10] Risk factors for fungal peritonitis include recent antibiotic therapy, frequent episodes of bacterial peritonitis and immune-suppression. In our study, no fungal peritonitis was seen. It may be due to difficulty in fungal culture and small sample size.

In the current study, 85% episodes were solitary, whereas 15% accounted for recurrent (5%), refractory (5%) and repeat (5%) peritonitis. Similar results were found in a study by Pindi et al from India where 81% cases were solitary. In our study, there was one recurrent peritonitis episode which was culture negative. Refractory peritonitis episode showed growth of Acinetobacter iowfii which was resistant to Ceftazidime and all other antibiotics. PD catheter was removed and patient was switched to HD in that case. Repeat peritonitis showed growth of Klebsiella pneumoniae which was resistant to Ceftazidime but sensitive to piperacillin-tazobactum and meropenem. Nessim et al found that the first peritonitis episode was associated with the formation of biofilm on PD catheter which puts patients at increased risk of subsequent infection due to difficulty in eradication of micro-organisms.[19]

Our study showed overall primary cure rate of 95%. Catheter removal was done in 1 (5%) case which was due to Klebsiella pneumonia and the patient was switched to hemodialysis. There were no deaths in our study population. In a study by Pindi et al overall primary cure rate was 77%; catheter removal was done in 15% cases due to relapsing peritonitis (6%), refractory peritonitis (4%) and refractory peritonitis (4%); mortality was seen in 2% cases due to septicemia.

CONCLUSION

In our study, more than half of CAPD episodes were due to Gram-negative organisms. Most common symptoms were abdominal pain and cloudy peritoneal effluent. Gram-negative peritonitis was associated with adverse outcome including increased duration of hospitalization and need for removal of catheter. Most of the patients recovered while few needed removal of catheter along with switch to hemodialysis

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CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

AUTHOR CONTRIBUTIONS

- Jagadish Pandey: Research concept, design, literature review, research experiment, data collection, analysis, statistical analysis, manuscript preparation
- Mahesh Raj Sigdel: Research concept, design, manuscript preparation
- Mukunda Prasad Kafle: Research concept, design, manuscript preparation
- Dibya Singh Shah: Research concept, design, literature review, research experiment, manuscript preparation

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