Peritonitis and Exit Site Infections in First Nations Patients on Peritoneal Dialysis

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Background and objectives: First Nations (FN) patients on peritoneal dialysis experience poor outcomes. Whether discrepancies exist regarding the microbiology, rate of infections, and outcomes between FN and non-FN peoples remains unknown.

Design, setting, participants, & measures: All adult peritoneal dialysis patients (n = 727) from 1997 to 2007 residing in Manitoba, Canada, were included. Parametric and nonparametric tests were used as necessary. Negative binomial regression was used to determine the relationship of rates of exit site infections (ESIs) and peritonitis between FN and non-FN peoples.

Results: A total of 161 FN and 566 non-FN subjects were included in the analyses. The unadjusted relative rates of peritonitis and ESIs in FN subjects were 132.7 and 86.0/100 patient-years compared with 87.8 and 78.2/100 patient-years in non-FN populations, respectively. FN versus non-FN were more likely to have culture-negative peritonitis (36.5 versus 20.8%, P < 0.0001) and Staphylococcus ESIs (54.1 versus 32.9%, P < 0.0001). The crude and adjusted rates of peritonitis were higher in FN subjects for both total episodes and culture-negative gram-negative peritonitis. Catheter removal because of peritonitis was similar in both groups (42.9 versus 38.1% for FN and non-FN subjects, respectively; P = 0.261).

Conclusions: FN patients experience higher rates of peritonitis and similar rates of ESIs compared with non-FN patients. Interventions to improve outcomes and prevent infections should specifically be targeted to the FN population.


T here has been a rapid rise in the prevalence of First Nations (FN) people with ESRD, largely because of epidemic rates of diabetic nephropathy (1–4). As a result, there is an increasing use of renal replacement therapy, with an eightfold increase in the number of prevalent Canadian FN patients on dialysis between 1980 and 2000 (5,6). Peritoneal dialysis (PD) is an attractive modality for these patients, given the remoteness of many of the FN communities. Recent data suggested that fewer FN people are initiating PD, with a trend toward higher risk for technique failure compared with whites (7,8). Data from Australia and New Zealand suggest peritonitis may account for the bulk of these technique failures (9).

Few data exist on the rates of peritonitis among Canadian FN populations and the impact it has on the maintenance of PD. Manitoba is unique because it has a very high rate of ESRD and FN patients. Using linked data from three sources (Manitoba Renal Program [MRP] Database, Canadian Organ Replacement Registry [CORR], and Peritonitis Organism Exit sites Tunnel infections [POET] database), we report the rates of peritonitis and exit site infections (ESIs), microbiology, and time to technique failure among FN and non-FN populations in Manitoba from 1997 to 2007.

Materials and Methods

Study Population and Design

The study population consisted of all adults (≥18 years of age) with ESRD who initiated PD between January 1, 1997 and December 31, 2007. Patients were followed until June 30, 2009 (Figure 1).

Data Sources

Local ethics board approval was obtained for database linkages. There are roughly 1200 prevalent dialysis patients in Manitoba, with 20% on PD. The MRP supplies clinical care and captures prospective data on patient demographics, comorbid illness, date of dialysis initiation, modality, technique failure, peritonitis, and death. Data acquisition for the MRP database is a structured process: the MRP registry is prospectively collected and updated weekly with respect to dates of dialysis initiation, modality transitions, and outcomes (peritonitis, technique failure, and death). The outcomes are adjudicated at a multidisciplinary weekly meeting attended by all renal healthcare providers (nephrologists, nurses, allied health). All modality changes, dialysis initiation, and deaths are cross-validated with billing data, which are captured separately and independently by the program. Furthermore, all outcomes were cross-validated against the CORR and POET databases. CORR is a national database that collects information on ESRD patients in Canada (5). POET is a North American, industry-supported database that collects information regarding PD-related infections and modality transfers (10). In
versus separated patients into FN
the event of discrepancies, additional data were obtained by chart
KT/V; PET, peritoneal equilibration test.
BMI, body mass index; pKT/V, peritoneal KT/V; rKT/V, renal
mellitus; CAD, coronary artery disease; CHF, congestive heart
Patient flow and cohort development. Dm, diabetes
urea and creatinine excretion. Greater than 90% of values for PET,
Kt/V used for analyses were the first recorded value after patients
mellitus was either type 1 or 2. Race was identified by self-report. For the purpose of this study, we
separated patients into FN versus non-FN, where the majority of
non-FN patients were white. Diabetes mellitus was either type 1 or 2. Coronary artery disease was defined as any of the following: the
presence of coronary artery disease by angiography, a positive stress test, or documented history of an acute coronary syndrome or coronary
artery bypass surgery. Congestive heart failure was defined by history of pulmonary edema by imaging. Peripheral vascular disease was
defined by ankle brachial index <1.0 or stenosis on angiography. Stroke was defined by radiographic demonstration of a cerebral ischemic event, hemorrhage, or history of transient ischemic attack. Active cigarette smoking or hypertensive medication use was determined at
the time of dialysis initiation. The date of PD initiation was recorded as the
date of peritoneal dialysis catheter insertion. Distance in kilometers
was calculated from the postal code obtained at the start of dialysis
initiation by ArcView v 9.3 (ESRI) using Vincenty’s formula (11). The
distance obtained represents the direct linear distance from the pa-
ient’s postal code to our major PD hospital in Winnipeg, MB, Canada,
resided a greater distance from their primary PD hospital com-
pared with the non-FN cohort. Diabetes mellitus was the most
common cause of ESRD in both groups but was almost twice as
common in the FN cohort (65.2 versus 38.7%).

Results
During the study period of January 1, 1997 to December 31,
2007, 727 (161 FN and 566 non-FN patients: 480 white, 61 Asian,
10 black, and 15 other/unknown) patients started PD in Mani-
toba, Canada. Total patient-years on dialysis were 400 and 1380
for FN and non-FN patients, respectively. Table 1 compares the
baseline characteristics of the FN and non-FN cohorts. FN
patients were more frequently women, younger, obese, and
resided a greater distance from their primary PD hospital com-
pared with the non-FN cohort. Diabetes mellitus was the most
common cause of ESRD in both groups but was almost twice as
common in the FN cohort (65.2 versus 38.7%).

Peritonitis
During the study period, there was a total of 986 episodes of
peritonitis in 393 patients (total peritonitis rate, 55.5/100 pa-
tient-years).

The microbiology of peritonitis in both cohorts is presented in
Figure 2. Staphylococcal infections were more frequent in the
non-FN cohort compared with the FN cohort (38.5 versus 19.8%,
P < 0.0001). Our peritonitis rate of methicillin-resistant Staph-
Staphylococcus aureus infection was very low (<10 cases), so it was not included in further analyses. Culture-negative peritonitis (20.8 versus 36.5%, P < 0.0001) was less frequent in non-FN patients. The unadjusted and adjusted relative rates of peritonitis are presented in Tables 2 and 3. The total peritonitis rate was significantly higher in the FN cohort (132.7/100 patient-years on PD [95% confidence interval, 106.6 to 158.8] versus 87.8/100 patient-years on PD [95% confidence interval, 77.8 to 97.9], P = 0.002). This effect persisted after adjustment for baseline differences between the two populations (101.9/100 patient-years on PD [95% confidence interval, 68.6 to 135.2] versus 64.6/100 patient-years on PD [95% confidence interval, 48.8 to 80.4], P = 0.012).

The relative rates of peritonitis by causative organisms are also presented in Tables 2 and 3. The rate of culture-negative peritonitis was significantly higher in the FN cohort (49.9/100 patient-years on PD [95% confidence interval, 37.5 to 62.4] versus 19.3/100 patient-years on PD [95% confidence interval, 15.7 to 22.8], P < 0.0001). In addition, rates of gram-negative peritonitis were higher in the FN populations (21.8/100 patient-years on PD [95% confidence interval, 14.7 to 29.0] versus 13.2/100 patient-years on PD [95% confidence interval, 10.4 to 16.2], P = 0.029). This effect persisted after adjustment for baseline characteristics (28.5/100 patient-years on PD [95% confidence interval, 13.0 to 44.0] versus 13.1/100 patient-years on PD [95% confidence interval, 7.5 to 18.3], P = 0.030). The relative rates were consistent across all four models that adjusted for various factors (Table 3).

ESIs

During the study period, there was a total of 815 ESIs in 373 patients (total ESI rate, 45.9/100 patient-years). The microbiology of ESIs is presented in Figure 3. Staphylococcus infections were more frequent in the FN cohort compared with the non-FN cohort (54.1 versus 32.9%, P < 0.0001). The unadjusted and adjusted relative rates of ESIs are presented in Tables 4 and 5. The total ESI rate was similar among FN and non-FN cohorts in both unadjusted and adjusted analyses.

When reported by causative organism in Tables 4 and 5, the rate of S. aureus ESIs was significantly higher in the FN cohort (40.9/100 patient-years on PD [95% confidence interval, 30.3 to 51.5] versus 25.1/100 patient-years on PD [95% confidence interval, 17.5 to 33.7], P = 0.002). This effect persisted after adjustment for baseline characteristics (28.5/100 patient-years on PD [95% confidence interval, 13.0 to 44.0] versus 13.1/100 patient-years on PD [95% confidence interval, 7.5 to 18.3], P = 0.030). The relative rates were consistent across all four models that adjusted for various factors (Table 5).

Table 1. Baseline demographics, cause of ESRD, comorbidities, and peritoneal dialysis characteristics of native and non-natives

<table>
<thead>
<tr>
<th></th>
<th>First Nations</th>
<th>Non-First Nations</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>161</td>
<td>566</td>
<td></td>
</tr>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female sex</td>
<td>87 (54)</td>
<td>238 (42.0)</td>
<td>0.009</td>
</tr>
<tr>
<td>age</td>
<td>49.2 ± 13.1</td>
<td>56.7 ± 15.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>body mass index</td>
<td>28.19 ± 5.13</td>
<td>26.57 ± 5.34</td>
<td>0.001</td>
</tr>
<tr>
<td>distance from centre (km)</td>
<td>249.5 (intraquartile range, 16.0 to 583.3)</td>
<td>7.4 (intraquartile range, 3.1 to 44.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cause of ESRD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>105 (65.2)</td>
<td>219 (38.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>glomerulonephritis</td>
<td>28 (17.4)</td>
<td>102 (18.0)</td>
<td>0.908</td>
</tr>
<tr>
<td>hypertension</td>
<td>11 (6.8)</td>
<td>67 (11.8)</td>
<td>0.083</td>
</tr>
<tr>
<td>polycystic kidney disease</td>
<td>0</td>
<td>33 (5.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>obstruction</td>
<td>1 (0.1)</td>
<td>28 (4.9)</td>
<td>0.010</td>
</tr>
<tr>
<td>other</td>
<td>4 (2.5)</td>
<td>58 (10.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>unknown</td>
<td>12 (7.5)</td>
<td>59 (10.4)</td>
<td>0.295</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diabetes mellitus</td>
<td>105 (65.2)</td>
<td>224 (39.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>coronary artery disease</td>
<td>32 (19.9)</td>
<td>116 (20.5)</td>
<td>0.912</td>
</tr>
<tr>
<td>stroke</td>
<td>10 (6.2)</td>
<td>42 (7.4)</td>
<td>0.729</td>
</tr>
<tr>
<td>congestive heart failure</td>
<td>15 (9.3)</td>
<td>70 (12.4)</td>
<td>0.332</td>
</tr>
<tr>
<td>peripheral vascular disease</td>
<td>17 (10.6)</td>
<td>44 (7.8)</td>
<td>0.262</td>
</tr>
<tr>
<td>anti-hypertensive medication(s)</td>
<td>130 (80.7)</td>
<td>401 (70.8)</td>
<td>0.012</td>
</tr>
<tr>
<td>smoker</td>
<td>26 (16.1)</td>
<td>47 (8.3)</td>
<td>0.007</td>
</tr>
<tr>
<td>Peritoneal dialysis characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PET</td>
<td>0.730 ± 0.101</td>
<td>0.677 ± 0.117</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>pKT/V</td>
<td>1.65 ± 0.36</td>
<td>1.64 ± 0.39</td>
<td>0.785</td>
</tr>
<tr>
<td>rKT/V</td>
<td>0.66 ± 0.54</td>
<td>0.72 ± 0.55</td>
<td>0.257</td>
</tr>
</tbody>
</table>

Values in parentheses represent percentages, SDs, or intraquartile ranges. PET, peritoneal equilibration test; pKT/V, peritoneal KT/V; rKT/V, renal KT/V.
versus 20.8/100 patient-years on PD [95% confidence interval, 17.1 to 24.6], \( P < 0.0001 \), whereas the rate of *Staphylococcus epidermis* was higher in the non-FN populations (9.5/100 patient-years on PD [95% confidence interval, 5.1 to 13.9]) versus 15.2/100 patient-years on PD [95% confidence interval, 12.5 to 18.7], \( P = 0.027 \). After adjustment for baseline differences between the two populations, there was no significant difference in relative rates of gram-positive ESIs (54.6/100 patient-years on PD [95% confidence interval, 34.2 to 75.0]) versus 43.8/100 patient-years on PD [95% confidence interval, 31.9 to 55.8], \( P = 0.246 \). The sample size was too small to determine differences in *S. aureus* and *S. epidermis* ESIs in the adjusted data.

**Peritonitis and Catheter Loss**

The causes of catheter loss because of peritonitis are reported in Table 6. The rate of catheter loss caused by peritonitis was similar for both groups. However, when reported by causative organism, culture-negative peritonitis was associated with an increase in technique failure among FN patients (55.6 FN versus 34.4% non-FN, \( P = 0.02 \)), whereas *S. epidermis* was more common in the non-FN population. No differences caused by gram-negative organisms were detected.

**Discussion**

In our study of a large PD cohort, FN patients experienced a significantly higher rate of peritonitis, with differing causative microbiology. In contrast, the rates and microbiology of ESIs were similar in the two groups.

Our observed rates of peritonitis were similar to data from the Australia and New Zealand Data Registry in Australia. That study reported higher and comparable peritonitis rates among indigenous patients (115 episodes/100 patient-years on PD [95% confidence interval, 103 to 128]) compared with non-FN patients (60 episodes/100 patient-years on PD [95% confidence interval, 57 to 62]) (9). Higher rates of peritonitis are a reason for concern because they are associated with increased morbidity and mortality; however, they were not associated with increased catheter loss in our cohort (10). Recent data seem to suggest that FN patients on PD experience higher mortality overall; however, it is unclear whether the higher rate of peritonitis is causal (13).

FN patients experienced a high rate of culture-negative peritonitis in our study (36.5%), which is almost double the proportion deemed acceptable by the International Society of Peritoneal Dialysis guidelines (20%) (14). This is in contrast to previous reports from Australia and North America, where...
Table 2. Unadjusted relative rates of peritonitis by causative organism in First Nations and non-First Nations populations

<table>
<thead>
<tr>
<th>Organism</th>
<th>First Nations</th>
<th>Non-First Nations</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total peritonitis</td>
<td>132.7 (106.6 to 158.8)</td>
<td>87.8 (77.8 to 97.9)</td>
<td>0.002</td>
</tr>
<tr>
<td>Gram positive</td>
<td>43.7 (32.5 to 54.9)</td>
<td>46.4 (40.2 to 52.6)</td>
<td>0.682</td>
</tr>
<tr>
<td><em>Staph. epidermis</em></td>
<td>25.1 (17.4 to 32.9)</td>
<td>34.2 (29.2 to 39.3)</td>
<td>0.054</td>
</tr>
<tr>
<td><em>Staph. aureus</em></td>
<td>8.7 (4.5 to 12.8)</td>
<td>5.6 (4.0 to 7.6)</td>
<td>0.221</td>
</tr>
<tr>
<td><em>Streptococcus</em> sp.</td>
<td>16.4 (10.4 to 22.4)</td>
<td>9.7 (7.3 to 12.1)</td>
<td>0.042</td>
</tr>
<tr>
<td>Diphtheroids</td>
<td>1.8 (0 to 3.6)</td>
<td>3.1 (1.8 to 4.4)</td>
<td>0.234</td>
</tr>
<tr>
<td>Gram negative</td>
<td>21.8 (14.7 to 29.0)</td>
<td>13.2 (10.4 to 16.2)</td>
<td>0.029</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td>6.4 (2.8 to 9.9)</td>
<td>2.5 (1.3 to 3.7)</td>
<td>0.040</td>
</tr>
<tr>
<td><em>Pseudomonas</em></td>
<td>1.8 (0 to 3.6)</td>
<td>1.4 (0.6 to 2.3)</td>
<td>0.726</td>
</tr>
<tr>
<td>Culture negative</td>
<td>49.9 (37.5 to 62.4)</td>
<td>19.3 (15.7 to 22.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fungi</td>
<td>2.7 (0.5 to 4.9)</td>
<td>2.6 (1.4 to 3.8)</td>
<td>0.958</td>
</tr>
<tr>
<td>Multiple organisms</td>
<td>7.8 (3.8 to 11.7)</td>
<td>6.4 (4.5 to 8.3)</td>
<td>0.530</td>
</tr>
<tr>
<td>Other</td>
<td>7.3 (3.5 to 11.0)</td>
<td>1.4 (0.6 to 2.3)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Note: *Staph. aureus* includes only non–methicillin-resistant *Staphylococcus aureus*. Rate is presented as per 100 patient-years on peritoneal dialysis with 95% confidence intervals. Other includes unknown organisms, anaerobic organisms, no culture taken, and organisms identified by code only (e.g., cdc grp ef-48).

Table 3. Adjusted relative rates of peritonitis by causative organism in First Nations and non-First Nations populations

<table>
<thead>
<tr>
<th>Organism</th>
<th>First Nations</th>
<th>Non-First Nations</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total peritonitis</td>
<td>101.9 (68.6 to 135.2)</td>
<td>64.6 (48.8 to 80.4)</td>
<td>0.012</td>
</tr>
<tr>
<td>Gram positive</td>
<td>29.5 (17.2 to 41.8)</td>
<td>28.6 (19.8 to 37.4)</td>
<td>0.877</td>
</tr>
<tr>
<td>Gram negative</td>
<td>28.5 (13.0 to 44.0)</td>
<td>13.1 (7.5 to 18.3)</td>
<td>0.030</td>
</tr>
<tr>
<td>Culture negative</td>
<td>23.9 (12.0 to 35.8)</td>
<td>11.3 (6.7 to 15.9)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

Rate is presented as per 100 patient-years on peritoneal dialysis with 95% confidence interval.

Model A: adjusted for differences in baseline characteristics (age, gender, any exit site infection, body mass index, cause of ESRD, distance, history of diabetes mellitus, cigarette smoking and anti-hypertensive medication use).

Model B: adjusted for demographics (age, gender, body mass index, cause of ESRD, race, distance from center).

Model C: adjusted for comorbidities (congestive heart failure, cigarette smoking, coronary artery disease, stroke, peripheral vascular disease, anti-hypertensive medication use).

Model D: adjusted for peritoneal dialysis characteristics (peritoneal equilibration test, peritoneal KT/V, renal KT/V).
relative rates of culture-negative peritonitis were much lower (10,15). Neither study found that rates of culture-negative peritonitis differed based on racial origin. On average, our FN population resided in mostly rural areas, far from their primary PD hospital. This relative isolation may have adversely impacted adequacy of specimen collection and necessitated empiric antibiotic use before specimen collection (10,16). Interestingly, culture-negative peritonitis was associated with an increase in catheter loss, which contrasts with previous reports that found it to be a relatively benign infection (15,16).

After adjustment for demographics and comorbid illnesses, the rates of gram-negative peritonitis in the FN patients was higher compared with the non-FN patients. High rates of gram-negative isolates is concerning because it confers a worse prognosis, including recurrence, catheter loss, hospitalization, and technique failure (10,17–19).

The total ESI rate was similar among FN and non-FN populations and yielded the expected representation of gram-positive organisms (10). There were subtle differences in microbiology between the two groups. Specifically, the rate of *S. aureus*.
ESIs was significantly higher in the FN populations, whereas the rate of *S. epidermis* was higher in the non-FN populations. *S. aureus* ESIs have previously been shown to be associated with poor response to antibiotics, high rates of catheter removal, and tunnel infections, and therefore should be taken into account when planning preventative strategies for minimizing peritonitis (10).

Why are rates of peritonitis so high in the FN population? It is known that FN communities experience high rates of nasal colonization with *S. aureus*, clustering of *S. aureus* in families and communities, and higher rates of skin and soft tissue infections (20–22). This predisposition in turn may relate to a clustering in many FN communities of adverse social determinants of health, including low socioeconomic status, poor housing, domestic crowding, and lack of adequate plumbing and sewer infrastructure. Future studies might focus on the impact of these factors on peritonitis rates.

Our data can aid in determining strategies to prevent peritonitis in FN patients. Better surveillance for peritonitis, more intensive training and follow-up, improved sample collection protocols for individuals in remote FN communities, eradication of *S. aureus* nasal carriage, and improved health care, housing, water, and sewer infrastructure are all potential strategies for improving peritonitis rates in this high-risk group.

Our study has several limitations. First, we relied on registry data, the limitations of which include errors in physician or self-reporting, particularly for racial origin. We did not have patient level information regarding socioeconomic status, highest level of education, home visits by PD nursing staff, retraining episodes, anti-microbial susceptibilities, compliance with therapy, prior exposure to antibiotics, nasal colonization with *S. aureus*, prescribed peritoneal dialysate and technique, and peritoneal effluent culture method. This makes it difficult to identify causal factors predisposing this group to higher rates of peritonitis, negative cultures, and technique failure. We did not have data on how patients were selected for PD and whether discrepancies were present based on FN status. Other authors have reported a possible selection bias regarding FN patients and PD, and whether this occurred in our cohort could not be quantitated (6,23). Whether factors associated with choosing PD (e.g., living in an isolated community with poor infrastructure) are also confounding factors predisposing to peritonitis cannot be addressed with these data. Our high rate of culture-negative peritonitis may limit generalizability of these results to other PD practices.

In conclusion, FN patients on PD are at high risk of peritonitis, and this persisted after adjustment for known risk factors for peritonitis. Further studies are needed to identify what modifiable factors associated with FN status are responsible for this elevated risk. Ultimately, studies of interventions to improve outcomes and prevent infections should specifically target the FN population.

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**Disclosures**

M.M.S. has received educational speaker fees, honoraria, and/or served on advisory boards for Ortho Biotech, Servier, Amgen, Boehringer Ingelheim, Sanofi-aventis, Baxter, and Genzyme.

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