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Mycobacterium Tuberculosis Peritonitis in Peritoneal Dialysis Patients: A Scoping Review

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ABSTRACT

Background: The clinical syndrome of Mycobacterium tuberculosis (TB) peritoneal dialysis (PD) peritonitis is poorly understood. Whether local TB patterns modify the clinical syndrome, and what factors associate with poor outcomes is also unknown.

Methods: A scoping review identified published cases of TB PD peritonitis. Cases from low and high TB burden areas were compared, and cases that did or did not suffer a poor clinical outcome were compared.

Results: There were 216 cases identified. Demographics, presentation, diagnosis, treatment and outcomes were described. Significant delays in diagnosis were common (6.1 weeks) and were longer in patients from low TB burden regions (7.3 vs 3.7 weeks). In low TB burden areas, slower diagnostic methods were more commonly used like PD fluid culture (64.3 vs. 32.7%), and treatment was less likely with quinolone antibiotics (6.9 vs 34.1%). Higher national TB incidence and lower GDP per capita were found in cases that suffered PD catheter removal or death. Diagnostic delays were not longer in cases in which a patient suffered PD catheter removal or death. Cases that suffered death were older (51.9 vs 45.1 years) and less likely female (37.8 vs. 55.7%). Removal of PD catheter was more common in cases in which a patient died (62.0 vs 49.1%).

Conclusions: Outcomes in TB PD peritonitis are best predicted by national TB incidence, patient age and sex. Several unique features are identified to alert clinicians to use more rapid diagnostic methods that might enhance outcomes in TB PD peritonitis.

Keywords: Peritoneal Dialysis, Mycobacterium Tuberculosis, Peritonitis, Multi-drug Resistant Tuberculosis, High burden Tuberculosis country

Abbreviations

ESKD	End Stage Kidney Disease
GDP	Gross Domestic Product
ISPD	International Society of Peritoneal Dialysis
MTB/RIF	Mycobacterium tuberculosis/resistance to Rifampin
PD	Peritoneal Dialysis
TB	Tuberculosis
USD	United States Dollars
WHO	World Health Organization

Introduction

Patients with end-stage kidney disease (ESKD), on peritoneal dialysis (PD), have decreased cellular immunity.(1) This increases risk and prevalence of *Mycobacterium tuberculosis* (TB) infections, especially in endemic regions.(2) Peritonitis is the leading cause of PD technique failure,(3) and TB PD peritonitis often has an insidious presentation(4) with delayed diagnosis.(5) There remains a paucity of data regarding the presentation, management and outcomes of TB PD peritonitis, with prior studies limited to cases reports or case series from single countries. It is possible that the local TB patterns impact presentation, diagnosis or outcomes of TB PD peritonitis, but this has not been well studied. Furthermore, there remains uncertainty regarding factors predicting adverse outcomes, such as PD catheter removal or patient death,.

The World Health Organization (WHO) has identified 30 high TB burden countries that account for almost 90% of new TB cases, and criteria for low TB burden countries.(6) National health care systems have realigned priorities and resources to overcome the national TB burden.(7) However, national TB incidence may modify TB related outcomes independently of the identification of the WHO designation of high burden, since it correlates to the proportion of multi-drug resistant TB cases, and also to the local experience in management of TB. In contrast, high burden TB regions tend to be in less developed regions, which may affect access to diagnostic tests and medication treatments. However, whether national TB incidence rate, or the designation of high TB burden status affects demographics, presentation, diagnosis, management or outcomes of TB PD peritonitis remains uncertain.

Controversy remains regarding the optimal management strategies in TB PD peritonitis. An early International Society of Peritoneal Dialysis (ISPD) guideline recommended "catheter removal…necessary in all cases," (8) but the most updated ISPD guidelines fall short of making definitive recommendations on PD catheter removal, instead stating that "many patients respond to anti-tuberculous therapy without catheter removal".(9) Much of this uncertainty is due to the limitations of smaller published studies, and uncertainty regarding determinants of poor outcomes in TB PD peritonitis.

This scoping review had three objectives. Firstly, we described the demographics, presentation, diagnosis, management, and outcomes of TB PD peritonitis. Secondly, we compared cases of TB PD peritonitis in high versus low TB burden areas. Thirdly, we compared cases in which patients suffered or did not suffer removal of PD catheter removal or all-cause mortality.

Materials and Methods

Our protocol was developed using the recommended methodology for scoping reviews from the Joanna Briggs Institute.(10)

Search strategy and study selection criteria

A scoping review was performed using Cochrane, Embase, Medline, and Web of Science databases, with no date or language restriction. Search terms included "Peritoneal Dialysis," "Tuberculosis," "Mycobacteria," and "Peritonitis."

Studies were included if the study described a case of TB PD peritonitis. Cases of PD peritonitis caused by Mycobacteria that had not been confirmed to be tuberculosis were excluded, All patient ages were considered. All study types were included. References from review articles were screened to assure all cases were identified. Studies were included if they described at least one of demographics, presentation, diagnosis, treatment, or outcome of a TB PD peritonitis case.

Two authors (BT, BM) screened all titles and abstracts, and completed full text review, using Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). Conflicts were resolved by discussion and consensus between both authors (BT, BM).

Data extraction

Available data was extracted from each study for each case of PD TB peritonitis. Demographic data included country, age, sex, and cause of ESKD. Each country's TB incidence rate was recorded.(6) Presentation factors collected included timing (from initiation of peritoneal dialysis to symptoms, and from symptoms to diagnosis), symptoms, presence and location of extraperitoneal TB, and whether a patient completed treatment for bacterial peritonitis prior to diagnosis. The diagnostic data collected included the dialysate fluid count, whether it was polymorphonuclear or lymphocyte predominant, and the mechanism of diagnosis of TB PD peritonitis. Management and outcome data of interest included medication treatments, whether the peritoneal dialysis catheter was removed and all-cause patient mortality.

The burden of TB was defined as "low burden" or "high burden" as per the Global Tuberculosis Report of the World Health Organization (WHO).(6) Countries that were not identified to be either

"low burden" or "high burden" were considered "other." The GDP per capita was identified from the World Economic Outlook Database of the International Monetary Fund.(11)

We aspired to extract data regarding exposure to immunosuppressive medications, anti-tuberculous medication side effects or discontinuation rates, and the timing of PD catheter removal and mortality relative to the diagnosis of TB PD peritonitis. However, the case reports and case series included in this study rarely reported this data, and therefore it could not be summarized or described.

Data analysis: Objective One: Description of TB PD Peritonitis

The average for all demographics, presentation, diagnosis, management and outcomes for TB PD peritonitis cases was calculated. Factors that were continuous quantitative variables also had median and interquartile range calculated. The number of cases from which each factor could be collected was also reported.

Data analysis: Objective Two: Differences between low and high TB burden cases

Cases of TB PD peritonitis were compared between low and high TB burden countries. The average for all demographics, presentation, diagnosis, management and outcomes for TB PD peritonitis cases in low versus high TB burden countries were compared. Factors that were continuous quantitative variables also had median and interquartile range calculated. The number of cases from which each factor could be collected was also reported.

Data analysis: Objective three: Comparing cases that suffered adverse outcomes

Cases of TB PD peritonitis were compared between cases that did and did not suffer PD catheter removal or all-cause mortality. The average was reported for all factors, and for continuous quantitative variables, the median and interquartile range were also reported. The number of cases from which each factor could be collected was also reported.

For all data analysis, missing data was managed by complete cases analysis. We calculated p values using student t-tests for continuous variables and Fisher's exact test for categorical variables. However, p values are generally not reported for scoping reviews given the inherent data limitations such as publication bias. Therefore, we did not report p values in this study, but they are available on request.

Ethics

Ethics approval was not required as only pre-existing data of anonymized patients was collected for this study.

Registration

This trial was not registered since PROSPERO does not permit registration of scoping reviews.

Results

Search of MedLine, Embase, Cochrane and Web of Science databases yielded 198 references (Figure 1). After screening title and abstract, assessment for full-text eligibility, and removal of duplicates, 71 studies were included. There were 5 studies identified from review articles, for a

total of 76 studies, representing 216 cases of TB PD peritonitis for data extraction. Included studies are identified in the Supplementary References.

There were 20 countries from which 216 cases were reported (Table 1A), with national TB incidence rate ranging from 3 to 615 cases of tuberculosis per 100,000 population per annum. The GDP per capita ranged from 1,622 to 68,309 USD.

The low, other and high TB burden countries included 63, 73, and 80 cases, respectively (Table 1B). TB national incidence rate increased (7.0 to 48.8 to 187.1 cases per 100,000 per annum) and GDP per capita decreased (47,810 to 37,182 to 7,613 USD) from low to other to high TB burden countries.

Objective One: Description of TB PD Peritonitis

TB PD peritonitis does not show a significant sex preference (48.1% female)(table 2), and the average age is 48.9 years. The most common causes of ESKD are Diabetes mellitus (28.3%), glomerulonephritis (22.2%), and hypertension (17.2%). None of the cases reported patients' exposure to immunosuppression.

The interval between initiation of peritoneal dialysis and developing TB PD peritonitis is 20.3 months. There are significant delays from symptoms to diagnosis (average 6.1 weeks, median 4.0 weeks, IQR 5.3 weeks). The most common reported symptoms are abdominal pain (81.8%), fever (67.2%) and cloudy fluid (38.0%), but weight loss (27.7%) and hypercalcemia (3.6%) were also reported.

The majority of patients (68.5%) failed treatment for bacterial peritonitis prior to diagnosis of TB PD peritonitis. Extraperitoneal TB was found in almost a third of patients (30.1%) with lung being the most common site (21.1%).

The majority of cases (68.4%) had peritoneal dialysate fluid that was polymorphonuclear cell predominant at the time of diagnosis.

TB was identified most commonly by peritoneal dialysate fluid culture (57.1%) and peritoneal dialysate fluid smear (34.3%). Diagnostic techniques that lead to more rapid diagnosis were less commonly used, such as peritoneal dialysate PCR (9.3%), and peritoneal biopsy (18.6%).

Treatment of TB PD peritonitis was most commonly with rifampin (100.0%), isoniazid (99.1%), and pyrazinamide (81.7%). Quinolone antibiotics were used in a minority of cases (30.6%).

Peritoneal dialysis catheter was removed in 52.4% of cases, and 35.4% of cases resulted in all-cause mortality. Very few cases confirmed the cause of death, and thus we were unable to determine when death was related to TB.

Objective Two: Differences between low and high TB burden cases

Patients who developed TB PD peritonitis in low TB burden areas were older (56.3 vs 47.4 years) (Table 3), and less likely to have glomerulonephritis as the cause of ESKD (6.3% vs 22.7%). They had significantly longer delays to diagnosis (7.3 vs 3.7 weeks). Their symptoms were more likely

to include fevers (77.4 vs 33.3%) and less likely to have marked abdominal pain (54.5 vs 83.3%). There did not appear to be any difference in the rates of extraperitoneal TB between low and high TB burden regions (33.3 v 33.3%).

Peritoneal dialysate was PMN predominant in the majority of cases in low (68.4%) and high (84.2%) TB burden areas. Diagnosis in low TB burden areas was more likely by slow methods such as dialysate fluid culture (64.3 vs 32.7%) and less likely by the more rapid dialysate PCR (3.6 vs 14.3%). Diagnostic methods that require PD catheter removal were less common in low TB burden areas, such as PD catheter tip smear (0.0 vs 10.2%) and culture (1.8 vs 2.0%).

Low TB burden cases of TB PD peritonitis less often use ethambutol (34.5 vs 63.4%) or quinolone antibiotics (6.9 vs 34.1%).

Low TB burden cases of TB PD peritonitis have lower rates of PD catheter removal (55.7 vs 65.3%) and all-cause mortality (31.7 vs 47.9%).

Objective three: Comparing cases that suffered removal of Peritoneal Dialysis catheter

Patients with TB PD peritonitis who suffered PD catheter removal were more likely to be from areas with higher National TB incidence rate (123.3 vs 64.9 cases per 100,000 population per annum), and lower national GDP per capita (25222.0 vs 34805.2 USD)(Table 4). While there was no significant difference with age, fewer were female (47.1 vs 54.4%).

Patients with TB PD peritonitis who suffered PD catheter removal did not have significantly longer delays to diagnosis (6.2 vs 5.9 weeks). They were more likely to suffer from cloudy fluid (56.3 vs 26.2%), hypercalcemia (6.3 vs 0.0%) and less likely to have fever (41.7 vs 81.0%).

Extraperitoneal TB rates were similar (28.3 vs 26.9) in those who did and did not have PD catheter removal.

Cases in which PD catheter was removed had higher peritoneal dialysate cell counts (1406.7 vs 720.4 wbc/uL), but the majority of cases with or without PD catheter removal had dialysate fluid PMN predominance (77.4 and 67.7%, respectively).

Cases in which PD catheter was removed were more likely to have TB identified by mechanisms facilitated by PD catheter removal operation, such as PD catheter tip smear (7.7 vs 0.0%), PD catheter tip culture (1.3 vs 0.0%), and peritoneal biopsy (20.5 vs 8.3%).

Treatment for TB PD peritonitis did not significantly differ in those who did or did not suffer PD catheter removal.

All-cause mortality was higher in cases of TB PD peritonitis in which PD catheter was removed (36.5 vs 25.4%).

Objective three: Comparing cases that suffered all-cause mortality

Cases of TB PD peritonitis who died were from regions with higher National TB Incidence rate (118.5 vs 72.5 case per 100,000 population per annum) and lower national GDP per capita (25761.0 vs 32028.2)(Table 5). They tended to be older (51.9 vs 45.1 years), less likely female (37.8 vs 55.7%), and more likely diabetic (46.2 vs 23.1%).

There was not a significant difference in delays to diagnosis in those patients who did and did not suffer death (6.2 vs 6.1 weeks). Patients who died were more likely to have cloudy fluid (46.4 vs 34.8 %) and less likely to have fever (50.0 vs 68.1%).

There were no differences in the rates of extraperitoneal TB in those who did and did not suffer death (29.0 vs 26.6%).

The majority of patients with TB PD peritonitis who did and did not suffer death had dialysate fluid that was PMN predominant (81.5 and 70.2%, respectively).

There were no significant differences in the mechanism of identifying TB, nor in the treatment used. Rates of PD catheter removal were higher in cases of TB PD peritonitis in which a patient died (62.0 vs 49.1%).

Discussion

TB PD peritonitis varies considerably from bacterial peritonitis. Presentation is more insidious, with abdominal pain being absent in almost half of cases in low TB burden countries. Other signs such as weight loss and hypercalcemia are unique and suggestive of a longer disease course. While lymphocyte predominance in the dialysate fluid has previously been described in other series,(12) a predominance of polymorphonuclear (PMN) cells has also been reported,(13) and was identified in the majority of cases in this study, in both low and high TB burden areas. While neutrophils play a critical role in precipitating tissue damage in Mycobacteria tuberculosis infections,(14) the PMN predominance may reflect a milieu of chronic inflammation of the peritoneum.(15) Further study is required to better delineate the reasons for PMN versus lymphocyte predominance.

There are often significant delays before identification of TB as the infectious agent in TB PD peritonitis. In this study, this delay averaged 6.1 weeks from the onset of symptoms to diagnosis. Failure to respond to treatment for bacterial peritonitis was found in the majority (68.5%) of cases, and 30.1% of cases had evidence of extraperitoneal tuberculosis, with the most common site being pulmonary involvement. The majority of cases (52.4%) led to peritoneal catheter loss, and death rates (35.4%) were comparable to fungal PD peritonitis.(16) While smaller studies have previously reported that delays in diagnosis associate with increased mortality,(17) this study found no difference in the delay to diagnosis in patients who did or did not die from TB PD peritonitis. It is possible this discrepancy arose due to the larger data set used in this study. This study could not identify when PD catheter removal occurred due to treatment failure of traditional antibiotics, prior to diagnosis of TB PD peritonitis. Therefore, earlier diagnosis could potentially have prevented the adverse outcome of PD catheter removal in some cases in this scoping review.

Traditional diagnostic techniques used in PD peritonitis are limited in detection of tuberculosis. Smears of peritoneal dialysate for acid-fast bacilli are insensitive, and culture for TB often takes weeks to confirm diagnosis.(18) Laparoscopic peritoneal biopsy with histological evaluation is more than 90% sensitive and 90% specific,(19, 20) however laparoscopic risks such as bleeding and intraabdominal adhesions, while reported to be quite rare (< 0.1% cases)(21), may be increased in patients with ESKD.(18) Options for earlier detection include *Mycobacterium tuberculosis* nucleic acid amplification by PCR,(5) measurement of adenosine deaminase levels in the peritoneal dialysate fluid,(22) or specialized assays.(23) One may also consider repeat PD dialysate cultures and smears to enhance sensitivity in cases with high level of suspicion for PD TB peritonitis, although this strategy requires further study. One must maintain a high index of suspicion for TB PD peritonitis, especially given the adverse outcomes, and consider using one of the options for earlier detection when unique signs or symptoms are present.

This study identified that diagnosis of TB PD peritonitis is more commonly made by dialysate fluid culture in low TB burden regions. Since this technique is often associated with delayed diagnosis, this reinforces the importance of using alternative rapid diagnostic tests and having a high level of suspicion when presentation is suggestive of TB PD peritonitis. Based on this scoping review, there are multiple signs that should alert a health care provider to the possibility of TB PD peritonitis (Table 6). The majority of TB PD peritonitis cases failed treatment for bacterial peritonitis prior to diagnosis, and there are several factors that differ from typical cases of bacterial PD peritonitis. These include hypercalcemia (3.6%), fevers (67.2%), weight loss (27.7%), evidence of extraperitoneal TB (30.1%), and a lymphocyte predominant peritoneal dialysate

(31.6%). Symptoms in low TB burden countries were frequently without significant abdominal pain or cloudy fluid. In cases reported in low TB burden countries in which the patient's birth country was described (n=33), it was often (16/33) from an area with high TB incidence, such as India (12/33), Pakistan (1/33), Nigeria (1/33), Haiti (1/33) or Ukraine 1/33). If any of these clinical features is present, a clinician should consider use of a more rapid diagnostic technique, such as dialysate fluid PCR or the Xpert MTB/RIF assay, to facilitate earlier diagnosis and management.

This study identified several factors that were more common in TB PD peritonitis cases that suffered a poor outcome. Patients who died were more likely to be older and male. The relationship between age and TB mortality is well described.(24, 25) The relationship between sex and TB mortality has been extensively studied. Men have higher incident TB rates and higher mortality, although mortality is similar in areas with high HIV co-infection.(26) Women may be less susceptible to TB infection,(26, 27) However, this also reinforces the importance of more rapid and accurate diagnostic tools. The WHO recommends that the Xpert MTB/RIF assay "should be used as the initial test for TB diagnosis in people living with HIV or who are suspected of multidrug-resistant TB." This assay has also been effectively used in peritoneal dialysis fluid to identify TB rapidly.(23) A recent systematic review confirms the Xpert MTB/RIF, and Xpert Ultra have high sensitivity and specificity, especially in smear-negative patients.(28) Therefore, its utilization could be a mechanism to improve diagnostic speed, and to decrease mortality from TB PD peritonitis.

National TB incidence was higher in cases of TB PD peritonitis in which a patient died. This is likely due a number of factors. Firstly, this study identified that the use of quinolone antibiotics

was higher in high TB burden areas, reflective of established correlation between TB burden and rates of multidrug resistant TB.(29) Secondly, national TB incidence rate may correlate to higher rates of malnutrition and food insecurity.(30) It is important to note that cases in which a patient died had no greater delays in diagnosis and were not more likely to have failed treatment for bacterial peritonitis. Mortality may be most affected by factors such as patient age, sex and national TB incidence rate. Thirdly, a higher proportion of patients in high TB burden countries had glomerulonephritis as the cause of their ESKD. It is possible that increased mortality in these patients reflected less effective eradication of mycobacteria due to simultaneous immunosuppression. Unfortunately, immunosuppressive medications were not reported in the included cases, so this scoping review is unable to support or to refute this assertion.

It appears that the peritoneal dialysis catheter removal rate may be higher in those patients who died. This could simply reflect that patients who were more sick were more likely to have their PD catheter removed. On the other hand, this scoping review did not find evidence that PD catheter removal associated with an increased probability of survival. Similarly, the rates of death in patients who had their PD catheter removed was higher. While caution must be exercised given the significant limitations of this data, it does support the importance of assuring earlier diagnosis with enhanced diagnostic tools, and early pharmacologic (rather than surgical) management.

There were important differences in TB PD peritonitis depending on national TB incidence and TB burden designation. Cases in low TB burden countries had longer delays to diagnosis. While this could be simply due to the lower clinician suspicion given the decreased familiarity with TB, cases in low TB burden countries also had low rates of abdominal pain and cloudy fluid (15.2%),

which are considered typical symptoms for bacterial PD peritonitis. Given this atypical presentation, clinicians identifying this pattern should consider the possibility of PD TB peritonitis and organize more rapid testing. Indeed, the peritoneal dialysate fluid culture, a slow diagnostic technique, was the most common in low TB burden countries, suggesting the potential for shorter diagnostic delays and improved outcomes with more rapid diagnostic techniques.

This study had several strengths. Firstly, by combining data from multiple case reports and case series of PD TB peritonitis, this scoping review identified demographic, presentation, diagnosis, treatment and outcomes with a higher rigor, while identifying important differences depending on regional TB patterns. Secondly, this study identified clinical signs TB PD peritonitis that were unique, compared to bacterial peritonitis, thus triggering clinicians to increase clinical suspicion and to utilize more sensitive and rapid diagnostic techniques. Thirdly, this study identified more rapid diagnostic tools such as peritoneal dialysate fluid PCR or the Xpert MTB/RIF assay. Finally, this study identified difference between cases with and without poor clinical outcomes. Specifically, this study did not find evidence that PD catheter removal associated with improved survival. While this scoping review can't exclude the possibility that PD catheter removal may be beneficial in some cases, it does support the assertion that in many cases, PD catheter removal is not necessary and should not be considered empirically necessary. This study also identifies that mortality in TB PD peritonitis is best predicted by patient age, sex, and national TB incidence rates. There are several weaknesses to this study. Firstly, conclusions were made from paired data using an incomplete data set. Data was extracted from case reports and case reviews, and thus confounding factors that may have impacted outcomes were not consistently reported, such as peritoneal dialysis clearance, HIV status and background immunosuppression. Secondly, it is

possible that some cases were missed, and that the conclusions could be more confident with additional cases. Thirdly, the cause of death was not consistently reported,. Therefore, it is uncertain if patients who died suffered from TB-related cause of death. It is possible that mortality was modified by risks other than those that were reported in cases. Furthermore, diagnostic techniques may not have been standardized across studies. This is especially true for TB culture and smear, which are highly variable depending on the laboratory and testing technique. Finally, as a scoping review of case reports and case studies, there is significant reporting biases. On the other hand, the more complete collection of cases enabled consideration of differences in TB epidemiology and in cases with adverse clinical outcomes with a higher confidence. Future research questions could be established (Table 7). This would support consideration of an online case report database with open access to clinicians.

This study yields helpful insights into the demographics, presentation, diagnosis, treatment and outcomes of TB PD peritonitis, as well as the impact of national TB incidence rate and TB burden status on clinical outcomes. Adverse clinical outcomes are best predicted by patient age, sex, and national TB incidence rate. This reinforces the importance of modifying socioeconomic factors to enhance clinical outcomes, as recommended in the WHO Development Programme. Further research will be needed to determine how more rapid diagnostic techniques can alter the clinical outcomes of TB PD peritonitis in both low and high TB burden areas.

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Legend to Figure: None

Figure 1: PRISMA diagram for study inclusion

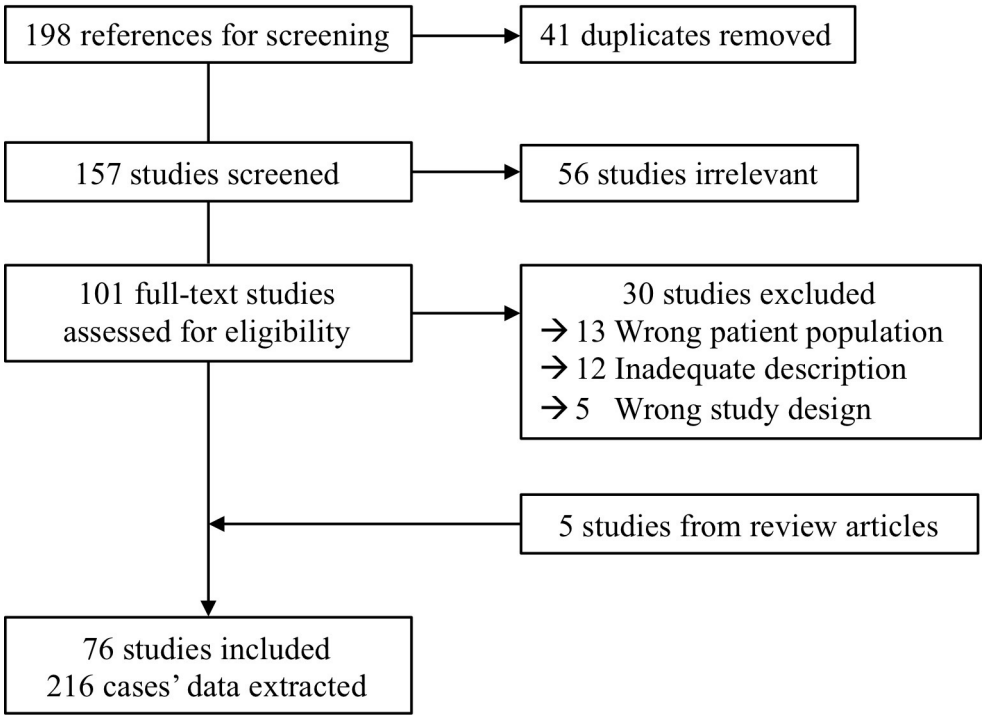

Figure 1: PRISMA diagram for study inclusion

NEP_13997_Figure 1 TBP copy.jpg

Table 1: Demographics of Cases of Mycobacterium Tuberculosis Peritonitis in Peritoneal Dialysis

1A. Country

Country Reported	Cases (n)	TB Incidence Rate (per 100,000 population per annum)	GDP Per Capita (USD)
High TB Burden Countries			
China	41	58	11819
South Africa	12	615	5444
India	27	193	2191
Low TB Burden Countries			
Austria	1	6	53859
Canada	3	6	49222
France	9	9	44995
Greece	1	4	19673
New Zealand	4	8	47499
Saudi Arabia	5	10	22700
Spain	8	9	30996
UK	16	8	46344
USA	16	3	68309
Other TB Burden Countries			
Hong Kong	42	63	48713
Japan	2	13	42928
Korea	1	59	34866
Malaysia	2	92	11604
Portugal	1	19	25065
Senegal	1	117	1622
Singapore	5	41	64103
Turkey	19	16	9327

1B. National Tuberculosis Incidence Rate

	TB Incidence Rate (per 100,000 population per annum)	Cases (n)	GDP Per Capita (USD)
Low Burden	7.0	63	47,810.6
Other	48.8	73	37,182.1
High Burden	187.1	80	7,613.3

Table 2: Tuberculosis Peritonitis in Peritoneal Dialysis: Demographics, Presentation, Diagnosis, Treatment and Outcomes

Factor	Cases reported (n)	Mean	Median	IQR
DEMOGRAPHICS				
Age	163	48.9	50.0	23.0
Sex (% Female)	162	48.1		
Etiology ESRD	99			
Diabetes mellitus		28.3		
Hypertension		17.2		
Glomerulonephritis		22.2		
Cystic diseases		4.0		
Urologic		7.1		
Other or Unknown		21.2		
PRESENTATION				
Starting Peritoneal dialysis to symptoms (Months)	143	20.3	12.0	21.9
Symptoms to diagnosis (weeks)	120	6.1	4.0	5.3
Symptoms and signs	137			
Abdominal pain		81.8		
Fever		67.2		
Weight Loss		27.7		
Cloudy Fluid		38.0		
Other Symptoms		12.4		
Hypercalcemia		3.6		
Failed treatment for bacterial peritonitis prior to diagnosis	82	68.5		
Extraperitoneal Tuberculosis	123			
Any site		30.1		
Pulmonary		21.1		
Lymphadenopathy		3.3		
Other		7.3		
DIAGNOSIS				
Cell count (wbc/uL)	76	1163.4	400.0	1030.0
Polymorphonuclear cell predominance	85	68.4		
Lymphocyte predominance	85	31.6		
Mechanism of Identification of Tuberculosis	140			
Peritoneal dialysate fluid smear		34.3		
Peritoneal dialysate fluid culture		57.1		
Peritoneal dialysate PCR		9.3		
Peritoneal biopsy		18.6		
Other		10.0		
Peritoneal dialysis catheter tip smear		3.6		
Peritoneal dialysis catheter tip culture		1.4		
TREATMENT	109			
Rifampin		100.0		
Isoniazid		99.1		
Ethambutol		45.9		
Pyazinamide		81.7		
Quinolone antibiotic		30.6		
Other		8.3		
OUTCOMES				
Peritoneal dialysis catheter removed	167	52.4		
All-cause mortality	206	35.4		

Table 3: Tuberculosis Peritonitis in Peritoneal Dialysis: Low versus High Tuberculosis Burden Cases

	Low TB Burden				High TB Burden			
Factor	**Cases reported (n)**	**Mean**	**Median**	**IQR**	**Cases reported (n)**	**Mean**	**Median**	**IQR**
DEMOGRAPHICS: Age	64	56.3	55.5	16.5	53	47.4	49.0	21.7
Sex (% Female)	63	46.0			53	45.3		
Etiology ESRD	32				44			
Diabetes mellitus		34.4				31.8		
Hypertension		12.5				18.2		
Glomerulonephritis		6.3				22.7		
Cystic diseases		6.3				4.5		
Urologic		12.5				2.3		
Other or Unknown		28.1				20.5		
PRESENTATION								
Starting Peritoneal dialysis to symptoms (Months)	58	17.8	12.0	11.5	42	26.2	24.0	28.0
Symptoms to diagnosis (weeks)	40	7.3	5.0	6.8	40	3.7	3.8	3.9
Symptoms and signs	33				30			
Abdominal pain		54.5				83.3		
Fever		77.4				33.3		
Weight Loss		15.2				26.7		
Cloudy Fluid		36.4				56.7		
Other Symptoms		18.2				20.0		
Hypercalcemia		9.1				6.7		
Failed treatment for bacterial peritonitis prior to diagnosis	42	61.5			15	86.7		
Extraperitoneal Tuberculosis: Any site	48	33.3			30	33.3		
Pulmonary		25.0				16.7		
Lymphadenopathy		4.2				6.7		
Other		8.3				10.0		
DIAGNOSIS: Cell count (wbc/uL)	20	663.7	300.0	240.0	36	897.9	441.5	514.0
Polymorphonuclear cell predominance	19	68.4			38	84.2		
Lymphocyte predominance	19	31.6			38	15.8		
Mechanism of Identification of Tuberculosis	56				49			
Peritoneal dialysate fluid smear		28.6				34.7		
Peritoneal dialysate fluid culture		64.3				32.7		
Peritoneal dialysate PCR		3.6				14.3		
Peritoneal biopsy		26.8				14.3		
Other		10.7				8.2		
Peritoneal dialysis catheter tip smear		0.0				10.2		
Peritoneal dialysis catheter tip culture		1.8				2.0		
TREATMENT	29				41			
Rifampin		100.0				100.0		
Isoniazid		100.0				100.0		
Ethambutol		34.5				63.4		
Pyazinamide		75.9				92.7		
Quinolone antibiotic		6.9				34.1		
Other		0.0				2.4		
OUTCOMES								
Peritoneal dialysis catheter removed	61	55,7			49	65.3		
All-cause mortality	63	31.7			71	47.9		

P values were calculated between groups, but not reported, as per standard statistical reporting for scoping reviews. Available on request.

Table 4: Tuberculosis Peritonitis in Peritoneal Dialysis with and without Catheter removal

Factor		Catheter Not Removed				Catheter Removed			
		Cases reported (n)	Mean	Median	IQR	Cases reported (n)	Mean	Median	IQR
National TB Incidence rate (cases per 100,000 population per annum)		71	64.9	58.0	55.0	96	123.3	41.0	184.0
National GDP per capita (USD)		71	34805.2	47499.0	39386.0	96	25222.0	11819.0	40900.0
DEMOGRAPHICS	Age	58	46.4	47.0	22.0	85	47.8	50.0	22.0
	Sex (% Female)	57	54.4			85	47.1		
Etiology ESRD		30				52			
	Diabetes mellitus		33.3				26.9		
	Hypertension		13.3				15.4		
	Glomerulonephritis		13.3				15.4		
	Cystic diseases		0.0				5.8		
	Urologic		10.0				7.7		
	Other or Unknown		23.3				23.1		
PRESENTATION									
Starting Peritoneal dialysis to symptoms (Months)		47	19.4	8.0	26.0	67	18.6	12.0	17.0
Symptoms to diagnosis (weeks)		47	5.9	4.5	4.5	69	6.2	4.0	6.0
Symptoms and signs		42				48			
	Abdominal pain		78.6				72.9		
	Fever		81.0				41.7		
	Weight Loss		14.3				8.3		
	Cloudy Fluid		26.2				56.3		
	Other Symptoms		9.5				16.7		
	Hypercalcemia		0.0				6.3		
Failed treatment for bacterial peritonitis prior to diagnosis		41	73.2			49	65.3		
Extraperitoneal Tuberculosis:	Any site	52	26.9			60	28.3		
	Pulmonary		25.0				20.0		
	Lymphadenopathy		23.1				3.3		
	Other		3.8				8.3		
DIAGNOSIS:	Cell count (wbc/uL)	24	720.4	400.0	1237.4	50	1406.7	410.0	1021.5
Polymorphonuclear cell predominance		31	67.7			53	77.4		
Lymphocyte predominance		31	32.3			53	22.6		
Mechanism of Identification of Tuberculosis		48				78			
	Peritoneal dialysate fluid smear		33.3				30.8		
	Peritoneal dialysate fluid culture		50.0				44.9		
	Peritoneal dialysate PCR		10.4				9.0		
	Peritoneal biopsy		8.3				20.5		
	Other		14.6				5.1		
	Peritoneal dialysis catheter tip smear		0.0				7.7		
	Peritoneal dialysis catheter tip culture		0.0				1.3		
TREATMENT		31				41			
	Rifampin		100.0				100.0		
	Isoniazid		96.8				100.0		
	Ethambutol		45.4				41.5		
	Pyazinamide		74.2				75.6		
	Quinolone antibiotic		22.6				26.8		
	Other		9.7				14.6		
OUTCOMES									
Peritoneal Dialysis Catheter Removed		71	0.0			96	100.0		
All-cause mortality		71	25.4			96	36.5		

P values were calculated between groups, but not reported, as per standard statistical reporting for scoping reviews.

Table 5: Tuberculosis Peritonitis in Peritoneal Dialysis Patients with and without death

Factor		Alive				Death			
		Cases reported (n)	Mean	Median	IQR	Cases reported (n)	Mean	Median	IQR
National TB Incidence rate (cases per 100,000 population per annum)		133	72.5	30.0	54.0	73	118.5	63.0	184.8
National GDP per capita (USD)		133	32028.2	30996.0	39386.0	73	25761.0	11819.0	42055.0
DEMOGRAPHICS:	Age	98	45.1	45.0	22.0	44	51.9	54.5	14.3
	Sex (% Female)	97	55.7			45	37.8		
Etiology ESRD		52				26			
	Diabetes mellitus		23.1				46.2		
	Hypertension		17.3				15.4		
	Glomerulonephritis		17.3				15.4		
	Cystic diseases		5.8				0.0		
	Urologic		7.7				7.7		
	Other or Unknown		28.8				15.4		
PRESENTATION									
Starting Peritoneal dialysis to symptoms (Months)		77	20.7	10.0	23.0	36	14.1	10.5	12.3
Symptoms to diagnosis (weeks)		79	6.1	4.0	4.0	35	6.2	6.0	5.5
Symptoms and signs		69				28			
	Abdominal pain		72.5				82.1		
	Fever		68.1				50.0		
	Weight Loss		15.9				10.7		
	Cloudy Fluid		34.8				46.4		
	Other Symptoms		13.0				28.6		
	Hypercalcemia		4.3				7.1		
Failed treatment for bacterial peritonitis prior to diagnosis		66	69.7			38	63.2		
Extraperitoneal Tuberculosis:	Any site	79	26.6			31	29.0		
	Pulmonary		20.2				22.6		
	Lymphadenopathy		5.1				0.0		
	Other		2.5				9.7		
DIAGNOSIS:	Cell count (wbc/uL)	50	1207.9	400.0	1080.5	22	953.6	445.0	1185.5
	Polymorphonuclear cell predominance	57	70.2			27	81.5		
	Lymphocyte predominance	57	29.8			27	18.5		
Mechanism of Identification of Tuberculosis		84				40			
	Peritoneal dialysate fluid smear		30.9				32.5		
	Peritoneal dialysate fluid culture		46.4				50.0		
	Perioneal dialysate PCR		9.5				7.5		
	Peritoneal biopsy		15.5				17.5		
	Other		10.7				5.0		
	Peritoneal dialysis catheter tip smear		1.2				12.5		
	Peritoneal dialysis catheter tip culture		1.2				0.0		
TREATMENT		73				33			
	Rifampin		100.0				100.0		
	Isoniazid		98.6				100.0		
	Ethambutol		42.5				54.5		
	Pyazinamide		86.3				72.7		
	Quinolone antibiotic		30.1				27.3		
	Other		6.8				12.1		
OUTCOMES									
Peritoneal Dialysis Catheter Removed		106	49.1			50	62.0		
All-cause mortality		133	0.0			73	100.0		

P values were calculated between groups, but not reported, as per standard statistical reporting for scoping reviews.

Table 6: Clinical Features Suggestive of Tuberculosis Peritonitis in Peritoneal Dialysis

Peritoneal dialysis peritonitis in high TB burden area
Peritoneal dialysis peritonitis in a patient previously from a high TB burden area
Failure to resolve after treatment for bacterial peritonitis
Lack of significant abdominal pain or cloudy fluid in low TB burden area
Evidence of Extraperitoneal Tuberculosis
Hypercalcemia
Presence of fevers or weight loss
Lymphocyte predominance of peritoneal dialysate

Table 7: Future Research Questions

1	What is the impact of reductions in national TB incidence on the presentation, diagnosis, management and outcomes of TB PD peritonitis?
2	What is the impact of improvements in GDP per capitaon the presentation, diagnosis, management and outcomes of TB PD peritonitis?
3	How does immunosuppression timing, medication choice and dose impact presentation and outcomes of TB PD peritonitis?
4	How does HIV co-infection effect the presentation, diagnosis, management and outcomes in TB PD peritonitis?
5	Does the use of more rapid diagnostic testing enhance clinical outcomes in TB PD peritonitis?
6	When a PD catheter is removed in TB PD peritonitis, does the timing of removal impact patient survival?